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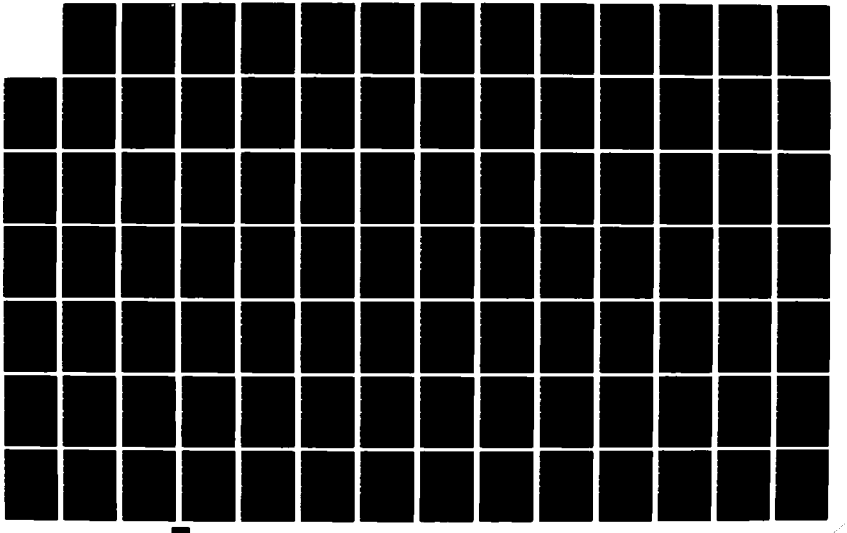

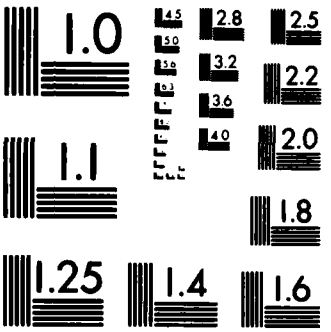

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THE EFFECT OF BETA ADRENERGIC BLOCKADE

ON RATINGS OF PERCEIVED EXERTION

Albert Anthony Hartzell, M.S., Captain, USAF

The University of Arizona, 1984

Director: Jack H. Wilmore

The purpose of this study was to describe the effect of beta blockade and endurance training on ratings of perceived exertion (RPE). Forty-seven healthy but sedentary male subjects, age 17 to 34 years, who were randomly assigned ~~on a double~~ blind basis to one of three groups, i.e. placebo, propranolol (160 mg/day) and atenolol (100 mg/day), and completed a 15-week endurance training program. Training responses were evidenced in all groups by increases in maximal oxygen uptake and ventilation, along with a reduction in maximal heart rate. For the same absolute work rate, RPE was significantly reduced post-training in both the blocked and unblocked conditions. However, RPE for the same relative work rate was unchanged in all three groups. Thus, beta blockade does not attenuate the normal physiological response to endurance training, nor does it affect RPE when expressed in relative terms. Therefore, RPE can be used in exercise prescription to monitor relative exercise intensity.

THE EFFECT OF BETA ADRENERGIC BLOCKADE ON RATINGS OF PERCEIVED EXERTION

by

Albert Anthony Hartzell

A Thesis Submitted to the Faculty of the

Committee on Animal Physiology (Graduate)

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_____ _____

Jack H. Wilmore
Professor of Physical Education

Date

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ABSTRACT

The purpose of this study was to describe the effect of beta blockade and endurance training on ratings of perceived exertion (RPE). Forty-seven healthy but sedentary male subjects, age 17 to 34 years, who were randomly assigned on a double blind basis to one of three groups, i.e. placebo, propranolol (160 mg/day) and atenolol (100 mg/day), and completed a 15-week endurance training program. Training responses were evidenced in all groups by increases in maximal oxygen uptake and ventilation, along with a reduction in maximal heart rate. For the same absolute work rate, RPE was significantly reduced post-training in both the blocked and unblocked conditions. However, RPE for the same relative work rate was unchanged in all three groups. Thus, beta blockade does not attenuate the normal physiological response to endurance training, nor does it affect RPE when expressed in relative terms. Therefore, RPE can be used in exercise prescription to monitor relative exercise intensity.

CHAPTER 1

INTRODUCTION

Cardiovascular disease (CVD) remains the most prevalent "killer" of the American population despite the advances which have been made in prevention and in the treatment and rehabilitation of its victims (1). Current estimates predict that at least 1.5 million new heart attacks will occur this year and at least one-third of these will die (1). Already, over 40 million people suffer from some form of heart or blood vessel disease and approximately 1 million people are added to the total each year (1). Obviously, the cost, time and energy needed to rehabilitate these people becomes astronomical.

Over the past ten years, significant strides have been made in the treatment and rehabilitation of patients with cardiovascular diseases. At least a part of this success can be attributed to the advent of cardiac rehabilitation and adult fitness programs. These programs have established the fact that most individuals can go through an aerobic training program and receive the proven physiological benefits of exercise. However, since many, if not most hypertensive and post-myocardial infarction patients are taking beta-adrenergic blocking medication, questions

have arisen regarding the trainability of these patients while they are under beta-adrenergic blockade. Several recent studies have shown a reduced exercise capacity and an inability to obtain a normal response to exercise training while under the influence of beta blockade treatment (2-3). Other studies have found no difference in the training potential of individuals who are under the influence of beta blockade as compared to a placebo-control group (4-11).

In a recent study by Ewy, et al. (4), a normal training response was found in a group of healthy subjects using the beta blocking agent sotalol compared to a placebo-control group following a 13-week training period. Pratt, et al. (5), using propranolol and a 3-month walk/jog training program, also demonstrated a training response in a group of cardiac patients.

If these and other positive findings regarding the use of beta blockers in combination with exercise rehabilitation are substantiated, then a more favorable approach to this form of therapy can be taken by those who have questioned the efficacy of using beta blockers and exercise training jointly in cardiac rehabilitation programs.

In anticipation of a more favorable trend in regards to joint therapy for cardiac patients, one must also consider the effects of beta blockers on exercise prescription. Current guidelines by the American College of Sports

Medicine (12) provide for the safe attainment of improved cardiovascular and musculoskeletal function by specifying an optimal mode, frequency, duration and intensity of exercise. Of these parameters, intensity as described by Shepherd (13) is the most critical. Intensity must be prescribed individually on the basis of the participant's graded exercise test (GXT). This allows the individual to participate safely in most activities without complications. Most cardiac rehabilitation and adult fitness programs prescribe exercise intensity by either the METS (1 MET=3.5 ml of oxygen per kg of body weight per minute) or the THR (target heart rate) methods. Upon inspection of these methods, it is obvious that the THR method is easier to use. THR is determined on the basis of the individual's resting and maximal HR (heart rate), and coupled together with the initial fitness level of the individual, it allows for an accurate prescription of exercise intensity.

The exercise HR can be monitored electrically or by the palpation of either the radial or carotid artery. The latter technique is accomplished by counting the number of pulse beats in a given time period. In a study by Chow (14), it was found that at 60% and 70% of maximal oxygen consumption ($\dot{V}O_2$ max), less than 1% error existed between: (a) palpated and exercise HR's, (b) palpated and immediate post-exercise HR's, and (c) immediate post-exercise and exercise HR's.

Chow (14) also discussed another method of monitoring HR. This method involves the use of ratings of perceived exertion (RPE) as described by Morgan and Borg (15) and Borg (16). Morgan (17) defined RPE as "one's subjective ratings of the intensity of work being performed" and stated that RPE is an indicator of one's relative physiological stress.

Since RPE is considered a useful indicator of the relative physiological stress, it may prove to be a useful monitor of the exercise intensity regardless of the health status of the individual. This becomes even more important when one considers that a number of cardiac and hypertensive patients are on beta blocking medication and/or are existing on "fixed" heart rates as a result of an implanted cardiac pacemaker. While most programs use the THR method for monitoring exercise intensity, Pandolf (18) states that the RPE method of monitoring exercise intensity has already proven useful in several adult fitness and cardiac rehabilitation programs. Chow (14), in an experimental study evaluating RPE and THR, noted that there were only minor differences in the accuracy of the two methods for prescribing exercise intensity. Therefore, the use of RPE in these programs could prove to be a viable alternative to the THR method of monitoring exercise intensity for those individuals who are under the influence of beta-blockade.

Statement of the Problem

This study was designed to investigate the influence of beta blockade, separately and in combination with an endurance training program, on ratings of perceived exertion during graded treadmill exercise. The primary objective was to examine the RPE response to exercise in normal, sedentary subjects consequent to chronic beta blockade, both before and after a 15-week endurance training program. A placebo control group, who also participated in the training program was used for comparative purposes. Furthermore, differences between cardioselective and nonselective beta blockers were evaluated.

RPE has been described as a useful indicator of the relative physiological stress (17) experienced during an acute bout of exercise. Thus, a secondary objective of this study was to examine the relationship of RPE to HR, $\dot{V}O_2$ and ventilation ($\dot{V}E$), observing the effect of beta blockade and training on these relationships at selected relative exercise intensities, i.e. 60%, 70%, 80% and 90% of $\dot{V}O_2$ max. RPE responses were differentiated into a "local" (leg), "central" (cardiorespiratory) and "overall" RPE rating to better describe these responses when influenced by beta blockade and endurance training. Finally, this study determined if RPE can be used as an effective monitor of exercise intensity while subjects are under the influence of beta blockade.

Hypotheses

1. Beta blocking agents will have little or no effect on the relationship of RPE to $\dot{V}O_2$ and $\dot{V}E$, either before or after training as compared to control conditions.
2. Beta blocking agents will cause a reduction in both resting and exercise HR and this will have an effect on the relationship of RPE to HR. Before training, RPE for the beta-blocked condition will not differ from the unblocked condition for the same work rate. After training, RPE under both blocked and unblocked conditions will be rated lower for the same work rate than before training, and there will be no difference between beta blockade and control conditions.
3. The differentiated ratings of RPE will result in a higher "local" rating than either "central" or "overall" RPE ratings both before and after training, as well as during beta blockade.
4. RPE can be used to safely monitor the exercise intensity while subjects are on beta blocking agents.

Assumptions

It was assumed that during all tests, each subject had a clear understanding of how to use the Borg scale which was used to determine RPE, that each subject received the same instructions and verbal encouragement, and that all subjects performed with a truly maximal effort in all phases of the testing and training. It was also assumed that there were no major changes in body composition and health status which would affect the outcome of this study.

Significance of the Study

This study proposes that traditional exercise training effects can be achieved by an individual while under the influence of beta blocking agents. If this hypothesis is confirmed, then a combination of beta blockade and exercise therapy would be the treatment of choice for most patients with cardiovascular disease. Subsequently, these patients should see an increase in their functional capacity, an improvement in their quality of life and a decrease in their risk of further cardiac involvement.

Beta blockade is known for its attenuating affect on HR and for the variability of this effect throughout a 24-hour period. Thus, THR would be difficult to define for these patients. Therefore, other means of monitoring the exercise intensity become necessary. RPE represents an easy to learn alternative which may prove to be an

effective means of monitoring the exercise intensity for individuals using beta blocking agents. The study of perceived exertion has grown immensely since Borg's (16) original thesis. It seems to have found its way into almost every aspect of the exercise physiology literature (18), and has proven to be a useful indicator of physiological stress (19). Therefore, the findings of this study should be of value in the prescription of exercise for individuals in cardiac rehabilitation programs.

This study also proposes to examine the relationships of RPE to several physiological variables in an effort to gain insight into the effect of beta blockade and training on these relationships.

CHAPTER 2

REVIEW OF LITERATURE

This chapter provides a review of the prevalence of cardiovascular disease, and a description of beta adrenergic blocking agents with an emphasis on studies which have used propranolol and/or atenolol with exercise. Also included is a review of the research concerning RPE with an emphasis on the effect of beta blocking agents on RPE, and sensory cues for RPE. A final section reviews those studies which have used RPE in the prescription of exercise.

Prevalence of the Problem

Provisional statistics for 1981 estimate that more than 42,000,000 Americans have one or more forms of heart or blood vessel disease (1). Individually, the major forms of disease are high blood pressure, 37 million; coronary heart disease (CHD), 4.6 million; rheumatic heart disease, 2 million; and stroke, 1.8 million (1). Cardiovascular disease resulted in 50% of all deaths (1) and current estimates predict another 1.5 million heart attacks for the year 1984 of which at least one-third will die (1). These numbers represent a substantial proportion of our

population and their rehabilitation and the prevention of future occurrences must be paramount in the minds of researchers and clinicians.

Effect of Physical Training in Normal Subjects and in Patients with Cardiovascular Disease

There are indeed many physiological changes which take place in the body during exercise. However, this section reviews only those changes associated with $\dot{V}O_2$, cardiac output ($\dot{Q}$), HR and stroke volume (SV).

Physical exercise has long been known to improve the quality of one's life. Physical training increases $\dot{V}O_2$ max in normal subjects. This increase is dependent upon the intensity and duration of training and the age and initial fitness level of the subject (20, 21). Within a relatively short period of time, a properly managed training program will enable participants to see positive changes in their body composition, exercise tolerance and their cardiovascular responses to the mode of exercise employed (22). In regard to the cardiovascular responses, adaptations in $\dot{V}O_2$ max, $\dot{Q}$, SV, HR, arterial-venous oxygen difference (A-$\dot{V}O_2$ diff) and $\dot{V}E$ have received the most attention in the literature.

$\dot{V}O_2$ max has been described by Sullivan and Froelicher (23) as the best indicator of aerobic work capacity and maximal cardiorespiratory function, and by Rowell (24) as the limit to the system's capability to

respond to an exercise stress. It can be altered by chronic physical exercise and by detraining as exemplified in bed rest studies (20, 25, 26). $\dot{V}O_2$ max is associated with the cardiovascular system by the following relationship: $\dot{V}O_2$ max = $\dot{Q}$ max·A-$\dot{V}O_2$ diff (max) where $\dot{Q}$ = SV·HR.

Normal, healthy subjects can generally achieve $\dot{V}O_2$ max values of 2.0 to 6.0 liters·min^{-1} and this measure of an individual's performance capability during strenuous exercise is highly reproducible (24). As individuals begin an acute bout of exercise, they will experience an increase in $\dot{V}O_2$. HR will also begin to rise linearly with $\dot{V}O_2$ in direct response to the intensity of the exercise, the total muscle mass involved, and the mode of the exercise employed (22). Hermansen (27) demonstrated the importance of the mode of exercise by showing that at an equivalent submaximal workload, the increase in HR is lower for walking with ski sticks than running, and lower for running than cycling. This then implies that if $\dot{V}O_2$ is the same for the different types of exercise, then the lower HR seen during exercise involving large muscle groups must be coupled with a larger SV since the relationship between $\dot{Q}$ and $\dot{V}O_2$ is the same for all types of exercise (28). Therefore, when comparing measurements in the same person, in which different modes of exercise are used, SV will be greater for leg exercise than for arm exercise at the same $\dot{V}O_2$ (28). However, SV during acute exercise plateaus at relatively

low levels of $\dot{V}O_2$ while the $\dot{Q}$ and HR continue to rise (24). When one now considers the effects of an aerobic training program, the latter statement concerning SV becomes even more important.

The effect of training (and detraining) on $\dot{V}O_2$ max, and in particular SV, is best exemplified by the now classic investigation by Saltin, et al. (20). In this study (20), $\dot{V}O_2$ max decreased by as much as 28% following 20 days of bedrest in sedentary subjects as compared to their pre-bedrest control value and increased by as much as 33% as compared to the pre-bedrest control value and 96% above the value obtained immediately after bedrest, when trained over a period of 3-6 months. In the same study (20) only a 2-8% increase in $\dot{V}O_2$ max was seen in their two well conditioned subjects. It would then be expected that the greatest increase in $\dot{V}O_2$ max should occur in subjects with the lowest initial values. Ekblom (21) verified the latter statement when he conditioned sedentary subjects and saw increases in $\dot{V}O_2$ max as high as 44%. However, in the same study (21) little or no change was seen in trained endurance athletes. This can be easily explained by the fact that when $\dot{V}O_2$ max is high, any change will be due primarily to an increase in SV. Therefore, the untrained subject can expect to see a decrease in their resting heart rate (HR rest) with little change in their maximal heart rate (HR max), an increase in their SV, and subsequently an increase

in both their peripheral ability to utilize more oxygen and their cardiac output. In the study by Saltin et al. (20) changes in SV accounted for all of the increase in $\dot{V}O_2$ max following training in the well conditioned athlete and all of the decrease in $\dot{V}O_2$ max following complete bed rest. In the untrained individual changes in SV will approximate 50% of the change in $\dot{V}O_2$ max with the remaining 50% coming from A-VO_2 diff (24).

When one now considers the patient with cardiovascular disease, their exercise training potential is usually approached with caution. Yet, many of these patients are similar to healthy subjects in their ability to train (28). It has been well established that endurance training will increase the $\dot{V}O_2$ max in patients with CHD with or without angina pectoris (28). However, in patients with angina pectoris the increase in $\dot{V}O_2$ max is symptom limited, therefore the increase will be smaller. Also, the absolute $\dot{V}O_2$ max will not be as great after training in patients with CHD, as compared to healthy subjects, due to their generally low initial values (28). Therefore, $\dot{V}O_2$ max can be improved by an increase in HR(max), SV(max) or A-$\dot{V}O_2$ diff(max) and since both normal subjects and patients with CHD (except those with angina pectoris or post myocardial infarction (MI) patients who see increases in HR max) experience either no change or a reduction in HR(max) after

training, the increase in $\dot{V}O_2$ max must be caused by an increase in either SV(max) and/or A-$\dot{V}O_2$ diff(max) (28).

Hagberg, et al. (29) studied 11 male cardiac patients both before and after twelve months of training. The first three months of exercise were similar to that of conventional cardiac rehabilitation programs. During the next 9 months, the patients exercised for one hour per session, 5 times per week at 70 to 90% of $\dot{V}O_2$ max. $\dot{V}O_2$ max was increased by 39% and SV during submaximal exercise at the same absolute and relative intensities was increased by 18%. An interesting aspect of this study was their calculation of stroke work. Stroke work is defined as the product of SV and mean arterial blood pressure (MAP). An increase in SV could be the result of a decreased MAP but in this study (29) there was an increase in stroke work. This indicates that the increase in SV was due more to central cardiac factors such as increased preload or increased contractility rather than the peripheral adaptations that have been seen in other studies. This study also demonstrates that longer, more intense training programs may be needed in order for CHD patients to obtain the desired physiological benefits of exercise training. Clausen (28) further points out that "the beneficial effects normal subjects and patients with CHD obtain from physical training are related to a more optimal circulatory regulation during submaximal exercise." In any event, both

normal subjects and patients with CHD must increase the training intensity to gain further improvement (22). Since it now seems that the cardiac patient can derive essentially the same physiological benefits as a normal subject, the next question concerns the interaction of exercise and beta adrenergic blocking agents.

Beta Adrenergic Blocking Agents

Exercise and beta blocking agents are two of the major forms of intervention in the treatment of cardiovascular diseases. The question is can these two mediators be combined effectively? First, however, it is necessary to examine the mechanism of action associated with beta adrenergic blocking agents (BABA).

The history of BABA dates back to 1906 where the first mention of receptors and their relation to the sympathetic nervous system (SNS) was made by Dale (30). In this now classic work, it was shown that sympathetic stimulation could be either excitatory or inhibitory. It wasn't until 1948 that Ahlquist (31) showed that there were actually two types of receptors, which he termed alpha (a) and beta (B), and one type of transmitter substance. Ahlquist (31) noticed that peripheral vasoconstriction, contractions of the uterus, bronchoconstriction and dilation of the pupils were all mediated by a-receptors; while B-receptors mediated the reverse of these actions. One of the principle actions of B-receptors are their action on the heart. Most notable

are the increases seen in contractility and rate. In 1964, Prichard and Gillam (32) investigated the potential of propranolol (Inderal), a BABA, in the treatment of hypertension. Then in 1967, Lands, et al. (33) described the existence of two B-receptor subtypes: B_1, whose primary effect was cardiac stimulation, and B_2, which caused bronchial and uterine relaxation and vasodilation.

Physiologically, the adrenal gland secretes both adrenaline and noradrenaline when stress of any type activates the sympathetic nervous system. This phenomena has been termed the "fight or flight" syndrome and it represents a defensive reaction which enables the body to increase its energy resources to meet the new demand. BABA oppose this mechanism by decreasing baseline levels of heart rate and blood pressure (BP) and attenuates their responses to stress, including exercise. Since these parameters are thought to be essential to induce those changes associated with exercise training, it is easy to postulate that there may be some difficulty for the cardiac patient to obtain a trained state while taking BABA. BABA have been proven effective in the treatment of cardiac and hypertensive patients and may prove to be of further value in combination with exercise therapy.

In this study, two BABA were used: propranolol, a non-selective agent, which blocks all B-receptor responses, and atenolol, a cardio-selective agent, which blocks

predominately B_1 receptors (34). Shand (34) has shown that small doses of propranolol (40 mg) and atenolol (50 mg) are basically indistinguishable as to their effect on heart rate, renin release and free fatty acids. Both of these BABA, as well as other BABA are used extensively in treating various cardiovascular diseases, including post-myocardial infarction patients.

Exercise induces sympathetic activity (35) and BABA attenuates it, therefore exercise is an excellent way to examine the effects of BABA on the normal sympathetic activity of the heart. Various studies have evaluated both selective and non-selective BABA and their actions on the exercising individual. According to McDevitt (36) the more cardioselective beta-blockers offer advantages for insulin-dependent diabetics and patients with obstructive airway disease. Cruickshank (37) also adds that cardioselective beta blockers possibly cause less fatigue in the exercising individual.

Beta blockade during acute exercise results in a reduction of HR, $\dot{Q}$ and BP for the same absolute level of work (38-40). The response to maximal exercise is equivocal and may be dose related (41-44) or possibly due to the cardioselectivity (44-46) of the BABA. In several studies (47-53), beta-blockade has been shown to decrease exercise capacity.

Hughson, et al. (47) investigated the effect of beta blockade using a single, 100-mg oral dose of metoprolol or matched placebo on 12 healthy males during both maximal cycle and treadmill exercise. Beta blockade significantly reduced $\dot{V}O_2$ max and HR max ($P<.0005$) on both ergometers. Folgering and Van Bussel (48), using six healthy male volunteers and a varying oral dose of metaprolol or placebo, found a significant reduction in maximal exercise power, i.e. the maximum absolute workload in Watts on the cycle ergometer. McFarlane, et al. (49) examined the response of five healthy males to propranolol both maximally and submaximally. Propranolol significantly reduced peak $\dot{V}O_2$, HR(max) and the maximum power output, i.e. the maximum absolute workload in Watts on the cycle ergometer. Bruce, et al. (50) used both healthy and cardiac impaired subjects and found that functional aerobic capacity was reduced with propranolol. Pearson, et al. (51) examined the acute effects of beta blockade on nine healthy adult male volunteers using propranolol and metoprolol. $\dot{Q}$ was measured at two steady state workloads (25 and 75 Watts) and once HR returned to close to resting values, a progressive maximum cycle ergometer exercise test was performed. Both drugs caused a 12% decrease in $\dot{Q}$ and a 3.5% decrease in oxygen consumption over the entire work range. In these studies and others (52, 53) the decrease in exercise capacity was evidenced by reductions in $\dot{V}O_2$ max, $\dot{Q}$

and exercise endurance time. Epstein and co-workers (53) explained that the fall in $\dot{Q}$ during submaximal work with BABA, was compensated by an increase in the A-$\dot{V}O_2$ diff, whereas in maximal work there was not a complete compensation and therefore $\dot{V}O_2$ max was reduced.

In still other studies (40, 54-56) no change was seen in $\dot{V}O_2$ max while the subjects were taking BABA. Ekblom, et al. (56) did not see any change in $\dot{V}O_2$ max while using BABA, but he did report a decrease in maximal $\dot{Q}$ and work time. Since there was a substantial decrease in the exercise HR, the results were explained by the compensatory mechanisms of SV and A-$\dot{V}O_2$ diff. In another study by Franciosa et al. (57) it was suggested that cardioselectivity is an important parameter as to the response during exercise. They found that $\dot{V}O_2$ max was decreased with propranolol (a non-selective agent) and unchanged with oxprenolol (a cardioselective agent). Wilmore et al. (58) reported only slight reductions in $\dot{V}O_2$ max using sotalol (a non-selective agent). Studies such as these (57, 58) suggest that selective agents such as atenolol (as used in the present study), will be found to be the beta blocker of choice when prescribing exercise for the cardiac patient. Support for cardioselective agents such as atenolol can be found throughout the literature for blood pressure reduction (59-62); heart rate reduction (61, 62); fewer plasma lipid disturbances (63); fewer effects on the central

nervous system, reaction times and mental concentration (64, 65); increased insulin sensitivity (45, 66); and less of a reduction of endurance exercise capacity (67).

Recently, investigators have looked at the combined effects of exercise training and BABA. In the study by Sable, et al. (2) no increases in $\dot{V}O_2$ max or maximal treadmill time were seen in a group of normal, sedentary males who underwent a five-week training program while using propranolol. Marsh, et al. (3) studied 12 healthy, sedentary, male volunteers who underwent maximal treadmill testing before and after a 6-week intensive aerobic exercise program. Six of the subjects received a 20 to 30 mg dose of propranolol, four times daily, in an effort to afford only partial blockade. The other six subjects received no medication or placebo and acted as a control. $\dot{V}O_2$ max increased in the control subjects but was unchanged in those receiving propranolol. Both groups realized an increase in exercise duration but the increase was greater in the control group. It was then concluded that beta blockade attenuated the normal response to exercise training.

Contrary to these studies, other investigators (4-11, 68-71) have seen more favorable results. In the study by Pratt, et al. (5) using cardiac patients, propranolol and a three-month training program, significant increases in $\dot{V}O_2$ max (estimated) and exercise duration were seen.

Horgan and Teo (6) examined the effects of beta blockade on 39 male cardiac patients who were aerobically trained three times a week for 8 weeks. Fourteen patients received acebutolol, 12 received sotalol and 13 received placebo, all on a double blind basis. Each group demonstrated significant improvements in exercise duration, energy expenditure, percentage functional aerobic impairment and heart rates attained while performing at equal work loads. No significant differences were found between the three groups either before or after training and it was concluded that beta blockade did not impair the normal response to exercise training. Welton, et al. (7) examined the effect of propranolol on nine cardiac patients as compared to 11 control patients all of whom underwent a 3-month walk/jog program. An increase in $\dot{V}O_2$ max was reported to be similar for the two groups and it was concluded that propranolol did not limit functional improvement in cardiac patients receiving exercise therapy as part of their rehabilitation.

Ewy, et al. (4) reported increases in both maximal oxygen uptake and treadmill time in twenty-seven healthy adult males after a 13-week training program using the beta blocker sotalol. An important point in this study is that the changes were not seen until after a 7 day post-medication period. It has been suggested by Ewy, et al. (4) that the differences seen in this study from that of Sable, et al. (2) could be due to either a drug specific

effect, different degrees of blockage or an inadequate training period. Nevertheless, these studies, as well as other recent evidence (8-11, 42) suggest that beta blockade does not alter the training response in cardiac patients (8) and may be both preferable and safer for this population (9).

Though the above review leaves many unanswered questions the use of exercise (68) and beta blockade (69-72) has made a significant impact on the rehabilitation of the cardiac patient.

Perceived Exertion

This section reviews some of the pertinent research involving ratings of perceived exertion (RPE). Several excellent reviews exist and the reader is referred to them for further insight (18, 19, 73, 74). This section will focus on the general concept of RPE, its relation to local and/or central factors, studies involving the use of BABA and the possible usefulness of RPE in the prescription of exercise.

General Concept

The original concept of perceived exertion was developed by Borg (16) and later refined by Borg (75). RPE have been described as a "gestalt" of sensations derived from both central (respiratory and cardiovascular) and peripheral or local factors, e.g. muscles, tendons, and

joints (19). Morgan (17) described RPE as one's subjective rating of the intensity of the work being performed. This subjective rating is based on a 15-point category scale (numbered 6 through 20) which is typically placed in front of the exercising subject. It is presented in quarto format (see Appendix D) and consists of verbal anchors at each of the odd numbers (e.g., 7=Very, very light; 9= Very Light;... 19=Very, very hard), and approximates the exercise HR by the relationship (HR=10 X RPE). Generally speaking, this relationship with HR holds true for submaximal stress (16) but it can be affected by the emotional state, age and health of the individual (76). Various investigators (16, 77-81) have consistently verified the linear relationship of RPE to HR, with reliability coefficients ranging from 0.76 to 0.90. Since there is a definite linear relationship between HR and RPE it would be assumed that a similar relationship exists between $\dot{V}O_2$ and RPE (82), and this relationship has also been verified (80, 83). Though most of the early work by Borg employed the cycle ergometer (16, 84), the same relationships hold true for the treadmill (85).

Local vs. Central Factors*

Borg (16) hypothesized that the effort sense was comprised of both local and central factors. But it was

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*Studies not using the Borg 15-point scale were deleted.

Ekblom and Goldbarg (86) who formally proposed the two-factor model. They also suggested that local factors provided the primary cue during effort while central factors were secondary. In agreement with Ekblom and Goldbarg (86), Pandolf (74) concluded that when a particular factor or physiological cue becomes accentuated by either an elevated rate, concentration or value, it can dominate the over-all rated perceived exertion. An example of this can be seen in the recent investigation by Young, et al. (87). In this study, differentiated RPE were obtained from eight low-altitude residents during cycle ergometer exercise at sea level and after acute (2 hours) and chronic (18 days) exposure to high altitude (4,300 meters). Local RPE was unchanged from sea level values after acute high altitude exercise. However, chronic high altitude exercise was associated with a significant reduction in the local RPE. At sea level, local ratings were significantly greater than central ratings but central RPE was highest during chronic high-altitude exposure. If the assumption made by Ekblom and Goldbarg (86) is correct it would seem reasonable to assume that local factors will dominate the overall RPE when under the influence of beta blockade, since BABA cause a decrease in baseline levels of HR.

Various studies (82, 86-106) have found RPE to be related to blood lactate (80, 86-92), kinesthetic cues (93,

94) and other local factors (95-104). Others (83, 105, 106) have disputed these relationships.

When central factors are considered, the literature is equivocal as to their role in the effort sense. Studies which have demonstrated central factor involvement have investiaged HR (79, 80, 83, 89, 90, 104, 105, 107), $\dot{V}E$ (80, 83, 86, 87, 92, 93, 101, 108-112), $\dot{V}O_2$ (80, 83, 89) and other central factors (90, 93, 99, 100, 103, 113-116, 123). Other studies have been unable to confirm central factor involvement with respect to HR (86-88, 93, 94, 97-99, 101, 102, 106, 109, 110, 116-125), $\dot{V}O_2$ (87, 93, 94, 99, 102, 106 110), $\dot{V}E$ (88, 93, 106, 122) and other central factors (88, 116) as primary cues in the effort sense.

Experiments which have manipulated HR (which are discussed in the next section) have provided perhaps the most solid evidence against the perceptual importance of heart rate as a central factor with a primary role in the effort sense (73). Robertson (116), in agreeing with Pandolf (74), suggests that central sensory cues may act as amplifiers in potentiating the local factors to the aerobic demand. Thus, local factors should dominate the effort sense in this study due to the attenuation of HR by the BABA.

Beta-Adrenergic Blocking Agents and RPE

As mentioned earlier, there is a high relationship between HR and RPE, but a number of studies have

manipulated the HR by using subjects of different ages (84), hypnosis (111), environment (87, 90, 101, 107, 109) and drugs (58, 86, 118, 125-128). Although there have been numerous studies involving BABA, Fellenius (124) points out that very few have involved the use of RPE.

Ekblom and Goldbarg (86) were among the first to use BABA in conjunction with the assessment of RPE. In this study, the effect of beta blockade on RPE was investigated in 14 healthy male subjects, seven of whom received propranolol (details of the effects of BABA on other physiological parameters can be found in Ekblom, et al. (46)). Propranolol decreased the HR max by an average of 38 beats·min^{-1} and HR for any given submaximal load was lower than the control values as evidence for the effectiveness of the medication. For any submaximal $\dot{V}O_2$, RPE was slightly, but not significantly, higher when blocked than in the unblocked state. RPE during maximal work remained unchanged while blocked, as compared to the unblocked maximal values and remained unchanged as compared to control values when related to O_2 deficit, ventilation and lactate concentration (86).

Davies and Sargeant (118) investigated the effect of practolol on four healthy male subjects and reported that RPE did not track HR during prolonged treadmill exercise, thus giving more credence to the concept that HR is not a primary sensory cue for the effort sense. Sjöberg,

et al. (125) examined the effects of a single intravenous dose of propranolol on 15 healthy male subjects. RPE at any given workload was slightly, but not significantly, higher while blocked as compared to the unblocked state. This conclusion is in agreement with that of Ekblom and Goldbarg (86) and further supports the notion that HR, which decreased after administration of propranol by 18-21%, is not a major determinant of one's perception of effort.

Grimby and Smith (125) investigated the effect of beta blockade on muscular strength in six healthy volunteers. The subjects were administered either placebo, propranolol (80 mg) or metoprolol (100 mg) in a double-blind, randomised manner. Before the muscle-strength tests were conducted, the subjects exercised on a mechanically braked bicycle ergometer for six minutes at 100 Watts. Although HR was significantly reduced for both drug groups, RPE was not affected. In a similar design, Van Herwaarden, et al. (127) examined the effects of beta blockade in 8 hypertensive patients. The non-selective BABA propranolol and the selective agent metoprolol were compared with a placebo in a double blind cross-over design. Measurements were taken during steady state exercise at an intensity that was considered moderate (1.5 Watts/kg body weight). Neither BABA influenced the RPE even though HR was reduced by 25%. Squires, et al. (128) investigated the effect of

propranolol on RPE in three groups of past myocardial revascularization surgery patients. Twenty-two patients received propranolol, 54 received no propranolol and 10 (two were on propranolol) were put into a hypotensive group. Each subject performed a symptom-limited GXT before hospital discharge. Submaximal and peak exercise HR was lower for the propranolol groups than the control group, but at matched exercise intensities RPE was the same. The hypotensive group failed to increase the systolic blood pressure (SBP) during exercise but at matched exercise intensities RPE was rated the same as the other two groups. These five studies (86, 118, 125-128) support the contention that HR is not a primary cue for the effort sense.

In the study by Pearson, et al. (51) single doses of propranolol (80 mg) and metoprolol (100 mg) were administered to nine healthy male volunteers aged 25-42 years who performed a progressive cycle ergometer exercise test. Both medications decreased HR by 35 beats$\cdot$min^{-1} and increased the RPE by 1.0 scale units over the whole range of oxygen consumption ($p<0.01$). Wilmore et al. (58) examined the effect of sotalol (320 mg/day for 7 days) in 28 healthy male subjects in a double blind, placebo-controlled study. Maximal HR decreased from 190 to 150 beats$\cdot$min^{-1} and they found no change in RPE which is in disagreement with Pearson et al. (51).

Karlsson (67) noticed that the same dose of propranolol induced a higher level of fatigue as measured by the percent impairment of jogging time, than atenolol. A significant covariation ($r=0.66$; $p<0.05$) was shown between the rated perceived peak exertion plotted on an individual basis versus peak impairment. This resulted in the propranolol group rating the same work with a higher RPE. The percent impairment of jogging time was also more pronounced in those subjects who were administered propranolol and who had a high percentage of slow twitch muscle fibers. Karlsson (67) suggests that the effect may be due to a heightened sensitivity to sympathetic nervous stimulation which may be dependent on heredity and/or endurance training. This suggests that there may be a difference in RPE due to dose, cardioselectivity and/or muscle fiber type.

In the recent literature, Tesch and Kaiser (129), have investigated RPE by differentiating the scores into a local (leg) effort and central (cardiorespiratory) effort. Propranolol (80 mg) was administered orally to 13 healthy, trained males, 2 hours prior to standardized maximal and submaximal exercises on an electrically braked cycle ergometer. The "local" RPE was rated higher than the "central" RPE both before and after beta blockade in both submaximal and maximal exercise. No differences were seen in either RPE rating while under normal conditions. The authors

conclude that the differences seen in the RPE ratings are most likely due to metabolic changes taking place within the skeletal muscle.

RPE and Exercise Prescription

Borg (130) reiterated the linear relationship of RPE to HR and the fact that RPE additionally integrates other variables of stress. This concept is the basis of the potential use of RPE in the prescription of exercise for cardiac patients, especially for those who have fixed heart rates or who are on BABA, and for normal healthy individuals. Pandolf (18) states that "it is hoped by clinicians that the regulation of the exercise intensity by RPE will allow for a safe exercise prescription when the limits for prescribed target HR must be strictly enforced." It has been suggested by Burke (131) and Morgan and Borg (132) that RPE could be used safely in the prescription of exercise for both healthy people and cardiac patients.

Earlier in this review, it was stated that cardiac patients could obtain essentially the same physiological training benefits as the normal, healthy individual. However, further improvement can only be realized by an increase in the training intensity (22). This fact in itself can lead to potentially dangerous heart rates. The cardiac patient on one hand may already have high resting heart rates which need to be controlled; on the other hand, any increase in training intensity will result in an acute

increase in the HR. Astrand and Rodahl (22) stress that intensive activities involving small muscle groups can produce excessively high heart rates and blood pressure in both cardiac patients and untrained but otherwise healthy individuals. Since the HR can be controlled by BABA, and since several investigators have suggested that RPE is not affected by BABA, the question that remains is can the subjective rating of perceived exertion be used to safely monitor the exercise intensity in the cardiac patient population?

Exercise intensity has traditionally been prescribed at a specific percentage of the individual's maximal effort. The most common methods for prescribing intensity have included the use of METS and THR. A MET is equivalent to the resting oxygen consumption or 3.5 $ml \cdot kg^{-1} \cdot min^{-1}$. An individual who has a 10 MET capacity would then have a $\dot{V}O_2$ max of 35 $ml \cdot kg^{-1} \cdot min^{-1}$. If this same individual was given an exercise prescription which required an exercise intensity equivalent to 70% $\dot{V}O_2$ max, then he/she would be required to work at 7 METS or 24.5 $ml \cdot kg^{-1} \cdot min^{-1}$. Though this method is relatively easy to use, it does not take into account the day to day physiological changes one would encounter upon entering an aerobic training program. Therefore, the prescription of exercise by the MET's method needs to be constantly re-assessed.

Another reliable method of prescribing the exercise intensity was introduced by Karvanen, et al. (130). This method is known as the THR method and is currently used by many cardiac rehabilitation and adult fitness programs. Wilmore (134) has described four advantages of using THR in the prescription of exercise: 1) it is applicable in all activities, 2) it controls for changes in conditioning level, 3) it can be used in any environment (heat, cold, et.), and 4) it can be used by anyone regardless of age, disability or level of conditioning. Currently, the American College of Sports Medicine (12) recommends exercise intensities of 60% to 90% of the maximal heart rate reserve, i.e. [(HR max - HR rest) X intensity + HR rest]. Since HR is easily palpated at the radial or carotid artery, this method is considered to be safe and reliable for most people. Still, other studies have investigated other means of prescribing the exercise intensity.

Recently, investigators have looked at additional methods of prescribing the exercise intensity which utilize various combinations of anaerobic threshold, HR and/or RPE. Purvis and Cureton (103) and Davis, et al. (135) suggest the use of anaerobic threshold in the prescription of exercise. In the study by Purvis and Cureton (103), they combined the use of anaerobic threshold and RPE and found that the anaerobic threshold corresponded to an RPE of

13.6±1.2. This value corresponds to the verbal anchor on the Borg scale "somewhat hard." They conclude that exercise intensity could then be prescribed by telling the individual to work at an intensity which they perceive as being somewhat hard. Though this method may have some merit, Yeh, et al. (136) reviews the difficulty associated with ascertaining the anaerobic threshold that various researchers have encountered. Therefore, if the subject can be taught how to use the Borg scale properly, then the use of RPE alone or in conjunction with HR in the prescription of exercise will save much time and effort.

One other method which seems to hold the most promise for the cardiac population is the use of RPE and HR combined. Morgan and Borg (15) predicted maximal exercise capacity in 20 adult males by using HR (multiple R=0.62) and RPE (multiple R=0.65) during a cycle ergometer test. By combining these two variables, the R then increased to 0.73. The authors suggested that this combined RPE-HR model was more accurate in the prediction of maximal exercise capacity and further suggested that this two-factor model might prove useful in the prescription of exercise (15).

Other investigators have also examined the use of RPE in exercise prescription. Burke (131) found that healthy participants in an adult fitness program, when working at moderate workloads (i.e. 65 to 80% $\dot{V}O_2$ max),

would consistently rate the work with an RPE of 13 and further suggested that RPE could be used to prescribe the exercise intensity safely in this population. Smutok, et al. (137) later tested 10 healthy adult males at established speeds and recorded their HR and RPE responses. The subjects then regulated the treadmill speed by their subjective responses. They found no difference in speed across all RPE between the 3 trials. However, during tests 2 and 3, HR became progressivly higher as speed and RPE decreased, which resulted in unreliable HR at walking speeds. Their conclusion was that exercise prescription by RPE was safe and reliable at heart rates above 150 beats·min^{-1} (80% HR max), an RPE above 12, and running speeds greater than 5.6 mph. However, the authors further suggested that exercise prescription below those limits was inaccurate and resulted in unreliable HR responses at the lower end of the Borg scale and could be potentially dangerous in the cardiac population. On the other hand, an RPE of 11 or below corresponds to a verbal rating of "fairly light" activity on the Borg scale and if the subject is instructed properly on its use there should not be a problem with excessively high heart rates at a low RPE.

Gutman, et al. (138) further extended the observations of Burke (131) and Smutok, et al. (137) to the cardiac population. This study involved 20 male cardiac patients who trained for 8 weeks following coronary by-pass

surgery and were stress tested at 2 and 8 weeks post surgery. The subjects were told to work as long and as hard as they could but not to exceed a pre-determined peak HR. Their RPE responses during training matched those recorded in their two graded exercise tests (GXT) and RPE matched HR within each trial, further suggesting that exercise intensity can be controlled by RPE. Still, Noble (139) suggests caution when prescribing exercise for the cardiac patient using perceptual sensations. Noble (139) stresses that the study by Smutok, et al. (137) asked subjects to reproduce a specific RPE, while Gutman, et al. (138) instructed the subjects to work at a tolerable level, but not a specific RPE and that these are two very different tasks. However, Noble (139) adds that it should be possible to control a THR by its associated RPE but this point needs further research.

Chow (14) elaborated on the point made by Noble (139) in her thesis. In her study, 29 healthy, college-aged males were randomly distributed into three groups. Group I was given a THR equivalent to 60 and 70% of their maximal capacity and were trained to use the palpation technique. They were then instructed to exercise within their THR range by using the palpation technique. Group II was trained to monitor their exercise intensity by RPE. A THR was also calculated for them but the subjects were not told what that range was in terms of HR. Group III acted

as a control group with no prescription. The results of Chow's investigation showed that the exercise intensity was maintained within the individualized THR ranges with an accuracy of 55.3%, 48.5% and 24.5% for Groups I, II and III respectively. This finding suggests that there was little difference between the accuracy of Group I (THR) and Group II (RPE) in regulating their exercise intensity to a prescribed level and that the RPE method may be a viable alternative to the THR method of prescribing the exercise intensity. Several other studies (140-144) have examined the potential use of RPE in the prescription of the exercise intensity but the results remain equivocal and therefore further research is needed.

From the majority of the above studies a trend can be seen in the potential use of RPE in the prescription of exercise. The present study proposes to evaluate the effects of BABA on RPE to better understand the interaction of these two variables. In the current literature, Sanders Williams, et al. (145) discusses the potential for unsupervised exercise programs for patients suffering ischemic heart diseases. Though RPE was not mentioned specifically, RPE may find its place within this context if its use can be validated and found to be reliable in both healthy and diseased populations. Morgan (17, page 97) put it aptly, "frequently, the important consideration is not what the individual is doing but rather what he thinks he's doing."

CHAPTER 3

RESEARCH METHODOLOGY

This chapter contains a comprehensive description of the subject population, their selection process and methods of drug administration and training. Also included are the methods of data collection and statistical analysis.

Subjects

Fifty-two adult, sedentary male subjects, aged 17-34 years, were selected from a larger group of volunteers on the basis of a medical questionnaire, a comprehensive physical examination, and an initial maximal exercise test. Forty-seven subjects successfully completed all aspects of the study. Physical characteristics of the subjects are presented in Table 1. The subjects were of an average level of fitness for their age (134) as is indicated by their mean, pre-training VO_2 max of 43.0 $ml \cdot kg^{-1} \cdot min^{-1}$. The medical questionnaire and physical examination revealed no contraindications to exercise as defined by the American College of Sports Medicine (12).

Criteria for exclusion from the study included the following:

Table 1. Physical, Cardiopulmonary and Metabolic Characteristics of the Subject Population

Variable	Placebo	Propranolol	Atenolol	Total
n	15	15	17	47
Age, yr	22.8± 4.7	24.3± 5.9	26.9± 4.5	24.8± 5.2
Height, cm	181.3± 8.0	178.7± 8.5	179.5± 5.9	179.8± 7.4
Wt, Kg-Pre	77.9±11.5	80.8±16.1	83.2±15.8	80.7±14.5
Wt, Kg-Post	75.9±10.2	78.6±16.0	81.3±15.3	78.7±14.0
Fat, %-Pre	18.3± 4.1	22.1± 8.7	23.1± 8.2	21.3± 7.5
Fat, %-Post	16.1± 3.6	20.4± 8.0	21.2± 8.0	19.3± 7.1
HR rest, $beats \cdot min^{-1}$	69.5±10.7	68.9±10.2	68.8±11.1	69.1±10.4
HR max, $beats \cdot min^{-1}$	197.0± 7.1	198.0± 7.8	199.7± 7.6	198.3± 7.4
$\dot{V}E$ max, $liters \cdot min^{-1}$	146.7±21.8	139.8±19.5	145.7±19.6	144.1±20.1
$\dot{V}O_2$ max, $ml \cdot kg^{-1} \cdot min^{-1}$	45.4± 4.5	42.4± 8.7	41.5± 5.6	43.0± 6.5

all values are means and standard deviations

1. Female
2. Relative body fat greater than 35.0%
3. History of significant cardiopulmonary disease or any of the following: asthma, gastrointestinal, hepatic, renal and/or hematological disease.
4. History of alcohol or drug abuse or factors which could adversely affect compliance or study procedures.
5. Clinically significant abnormal vital signs including pulse, respiratory rate, blood pressure or abnormalities in the physical examination.
6. Clinically significant abnormal electrocardiogram.
7. Subjects taking any medication.
8. Smokers.

Each subject was given a comprehensive description of the study in a one-hour lecture and in a brief written proposal. Informed consent was obtained in writing (Appendix A). The protocol was approved by the Committee on Human Subjects at the University of Arizona (Appendix B). Subjects were advised of their right to withdraw from the study without incurment of ill will. The physician in charge of this project reserved the right to withdraw medication from any subject when symptoms or signs of

adverse reactions were apparent. All adverse reactions were closely followed until completely resolved.

Drug Supplies

Propranalol (160 mg/day), atenolol (100 mg/day) and placebo were prepared, packaged (in matching tablets) and supplied by Stuart Pharmaceuticals. A randomized, double-blind assignment of medication was administered. All unused materials were returned to the company at the end of the study.

Methods

All subjects were given a complete medical examination in the two week period prior to the beginning of the study. Relative and absolute body fat and lean body weight were also determined during this period using the hydrostatic weighing technique (146), with the nitrogen dilution technique (147) being used to correct for air trapped in the lungs.

Submaximal and maximal responses to exercise testing were performed on a Quinton, Model 24-72 treadmill twice prior to initiating medication, to establish test reliability for each of the parameters measured. The specific protocol was designed to initially allow each subject to reach the state of volitional fatigue within 12 to 16 minutes. For the first control test, speed was kept constant at 3.5 mph and the grade, starting at 0°, was in-

creased by 3% every two minutes to the point of exhaustion. This protocol is described in Appendix C. During tests 2 through 5, the subjects completed a 20-min period of steady-state exercise at 60% of their $\dot{V}O_2$ max as determined from control test 1. This was followed by a rest period of five minutes, after which the subject continued exercising, resuming the protocol used in the first test.

A 12-lead electrocardiogram was monitored continuously during the first maximal treadmill test and heart rates were determined at the end of each minute. In subsequent tests, heart rates were monitored using a single lead, CM5 position. Blood pressures were determined by standard sphygmomanometry during each stage of the protocol except at the point of exhaustion. Submaximal cardiac outputs were measured during the steady-state exercise period at 60% $\dot{V}O_2$ max, using the CO_2-rebreathing technique as described by Wilmore, et al. (148). The treadmill grade for the steady-state exercise at 60% of VO_2 max was determined by linear regression of the $\dot{V}O_2$ and treadmill grade from the first control test. Measurements of $\dot{V}O_2$, $\dot{V}E$, FEO_2, $FECO_2$, and R were determined every 30 seconds using the Beckman Metabolic Measurement Cart (MMC) throughout each test. An evaluation of the MMC has been published by Wilmore, et al. (149).

Ratings of perceived exertion were differentiated into RPE_C (central), RPE_L (local), and RPE_O (overall). All

subjects were given the following instructions on the use of RPE before each exercise test in the study:

> You are about to take part in an exercise test that will measure several physiological variables. During this test you will be walking and/or running at progressively increasing workloads. As the workloads increase you will become more and more fatigued as you approach your maximum effort. This should be the point where you can not take another step and thus the end of the test. The scale you see in front of you is known as the "Borg Scale" and it measures your subjective ratings of the perceived exertion you feel and is referred to as RPE. During the test, we want you to be totally aware of all of your bodily sensations such as your breathing, heart rate, fatigue and/or pain in your muscles and joints, and basically how you feel overall. To these sensations we want you to put a numerical rating from the Borg Scale. As you can see, the scale begins with the number six and is the lowest sensation or rating you can have. An RPE of 6 is similar to sitting on a chair, totally relaxed. Each of the odd numbers are anchored with verbal expressions which are self-explanatory. However, we must point out that a rating of 20 is the absolute highest you can attain. It is virtually impossible to rate two workloads as a 20. This should be the endpoint of your test. No other ratings can be used. Therefore be aware of your bodily sensations throughout your work test. During each workload we will ask you for three ratings. I or another technician will ask for your central RPE (i.e., your perception of your heart rate and your breathing), your local RPE (i.e., sensations from your muscles and joints), and your overall RPE (i.e., integrate all of those sensations into one overall rating). The ratings can be different so be honest about how you feel during the test. Again, no rating can be lower than 6 or higher than 20.

Following the second maximal exercise test each subject was randomly assigned either propranolol, atenolol or a placebo, on a double blind basis. After one week on the medications a third maximal exercise test was performed. This test was used to assess pre-training beta blocker

activity and its effect on RPE and the acute responses to submaximal and maximal exercise, and to establish a training intensity between 70 and 85% of the subjects $\dot{V}O_2$ max.

Following the third maximal treadmill test, each subject began a supervised aerobic training program while still on medication. Each subject was required to initially walk, then jog or run as their fitness improved. The training program lasted 15 weeks and was conducted 5 days/week for a total of 75 training sessions. Initially, the training sessions consisted of 15 minutes of warm-up calisthenics and 30 minutes of walking and/or jogging. The training intensity was set at a training HR range between 70-85% of $\dot{V}O_2$ max as determined by the third maximal treadmill test. Training sessions were gradually increased in duration until at the end of the study, each subject could exercise for an entire one hour period. The subjects were instructed not to perform any additional formal exercise outside of that performed in the study.

Each subject could choose between three training sessions which were evenly spaced throughout the day so as not to conflict with work or school activities. When a subject missed an entire training day, he was required to either train on a supervised weekend session or to participate in two training sessions on one day in order to complete the required 75 exercise sessions. A careful record was made of the HR at the start of each session and at

15-minute intervals during the session. A log was also kept of the mileage covered, duration of the session, and the resting pulse rate upon rising each morning.

At the end of the fourteenth week, a fourth maximal treadmill test was performed and all measurements were repeated to assess any changes that might have occurred as a result of the training program while the subjects were still medicated. At this point all remaining medications were returned and the subjects were required to continue training for one additional week without medication.

Finally, a fifth maximal treadmill test was conducted at the end of the fifteenth week of training. Again all previously mentioned physiological variables were measured in an effort to establish a training response, post-medication.

Statistical Analysis

All data were analyzed using the Biomedical Statistical Package for two way analysis of variance using repeated measure (BMDP2V). When a difference between treatments (drugs) was observed, a simple analysis of variance was used to analyze mean difference scores across two trials, using the SPSS program. The Least Significant Difference (LSD) test was then used to determine those differences that achieved statistical significance. When a difference across trials was noted, the mean square error terms derived from the simple analysis of variance tests

were used to compute t-tests. Statistical significance was established at $p<0.05$.

CHAPTER 4

RESULTS

This chapter contains a brief synopsis of the subjects' attendance records and a brief review of the metabolic and cardiopulmonary responses to acute and chronic beta blockade, subsequent to a 15-week endurance training program. For the reader's convenience, several tables containing the actual data are presented in the appendix (Appendix E-J). Only those results concerning HR, VO_2 and VE will be reported. This chapter also contains a thorough analysis of the effect of beta blockade and endurance training on RPE.

Subject Compliance

Forty-seven of the original 52 subjects completed all phases of this study. Of the five subjects who did not complete this study, two sustained injuries early in the study, two quit due to lack of commitment and one left school and moved out of town.

Compliance with the training program was outstanding with the individual groups averaging between 96.7 to 98.2% attendance. During the first week of training, the groups averaged 13.3 to 15.3 miles per week in a time of

30.5 to 32.0 minutes per session. By the end of the thirteenth week of training, the groups were averaging 21.2 to 24.1 miles per week in a time of 44.0 to 45.0 minutes per session. This high rate of compliance and improvement in distance and time per session is partly due to each subject's willingness to be trained, the highly motivated exercise leaders who directed each training session, and the opportunity provided the subjects to attend one weekend make-up session each week.

Metabolic and Cardiopulmonary Responses

The results of this study are presented by referencing the following four tests and their relationships as follows:

C2 represents control test 2. Correlations and t-tests for determining the relationships and the significance of differences between Control test 1 and Control test 2 are presented in Table 2. As a result of the excellent agreement between these two tests, C2 was used for all further comparisons. C2 was also selected as the sole control test for comparison with the other three tests since its protocol was identical to those other tests. Control test 1 was strictly a maximal test.

Table 2. Correlations and t-tests for Control Test 1 vs. Control Test 2.

Variable	r	t-test
$\dot{V}O_2$ max	0.94	-1.24
Treadmill Time	0.93	4.46*
HR max	0.81	-0.51
$\dot{V}E$ max	0.78	-1.24
R max	0.44	0.45

*significant at the 0.05 level

Pre	represents the acute response to the medication prior to initiating training.
Post1	represents the first post-training test conducted while the subjects were still medicated.
Post2	represents the last test, conducted at the conclusion of training, one week after drug cessation.
Pre-C2	represents the differences in the acute responses to the medication compared to the unmedicated trial.
Post1-Pre	represents the training response while medicated.
Post2-C2	represents the training response unmedicated.
Post2-Post1	represents the changes which took place post-training, between medicated and unmedicated conditions.

The data are generally analyzed and presented on the basis of mean differences across trials to account for any differences which may have existed for the initial values between each treatment group (Placebo=PL, Propranolol=PR and Atenolol=AT).

Resting Responses

Resting cardiovascular responses to beta blockade and 15 weeks of endurance training are presented in Appendix E. As expected, acute beta blockade significantly

reduced resting HR (-11 and -15 beats·min^{-1} for PR and AT respectively). No significant differences existed between the two blocking agents. Training did not significantly affect HR at rest in any of the three groups. After drug cessation, HR returned to control levels in both of the blocked groups. Post1-Pre revealed no significant changes except for a further decrease in resting HR for the PR group. Post2-C2 revealed no significant training effects for any variable. After drug cessation, HR returned to control levels.

Submaximal Responses

The submaximal metabolic and cardiopulmonary data obtained during this study are presented in Appendix F through Appendix I. Pre-C2 comparisons revealed that beta blockade significantly reduced HR in the PR and AT groups equally at each submaximal relative intensity (Range- 42.4 to 50.2 beats·min^{-1} for both blocked groups at all intensities). $\dot{V}O_2$ was not significantly altered in the PL or PR groups at any workload. However, the $\dot{V}O_2$ in the AT group was significantly reduced at 60, 70 and 80% of $\dot{V}O_2$ max but was unchanged at 90% of $\dot{V}O_2$ max. VE was unchanged in the PL group, but significantly decreased in both of the blocked groups at 60% of $\dot{V}O_2$ max, significantly reduced in all three groups at 70% of $\dot{V}O_2$, significantly reduced in the AT group at 80% of $\dot{V}O_2$ max and significantly reduced in the PL and AT groups at 90% of $\dot{V}O_2$ max.

Post1-Pre comparisons depicted further significant reductions in HR across all three groups for each submaximal relative intensity. $\dot{V}O_2$ was unaltered in all three groups at each relative exercise intensity except for a significant increase at 80% of $\dot{V}O_2$ max in the PL group. $\dot{V}E$ was significantly reduced in all three groups at each relative intensity. The reduction of $\dot{V}E$ was generally greatest for the PR group.

Post2-C2 comparisons revealed significant decreases in submaximal HR for all three groups at each relative intensity. There were no significant differences in the magnitude of the reduction of HR between any of the three groups. Submaximal $\dot{V}O_2$ was not significantly altered in any of the groups. $\dot{V}E$ was significantly decreased at each of the submaximal relative intensities and in all three groups. The magnitude of this reduction in $\dot{V}E$ was generally greatest for the PR group. However, there were no significant differences in this training response between the three groups.

Maximal Responses

The maximal metabolic and cardiovascular changes resulting from beta blockade and training are presented in Appendix J. Pre-C2 comparisons revealed significant decreases in HR max of -49 and -44 beats·min^{-1} for the PR and AT groups respectively with no change noted in the PL group. $\dot{V}O_2$ max was unaltered by beta blockade. $\dot{V}E$ max was

significantly decreased by -15.9 and -12.1 liters·min^{-1} for the PR and AT group respectively, but was unchanged in the PL group.

Post1-Pre comparisons revealed significant reductions in HR max for the PL group, but was unchanged for the blocked groups, though there was a tendency toward a decrease. $\dot{V}O_2$ max and $\dot{V}E$ max were significantly increased in all three groups. However, the magnitude of the increase in $\dot{V}O_2$ max and $\dot{V}E$ max was significantly less for the PR group. These results indicate a classic response to training, even while medicated. Post2-C2 comparisons also revealed significant reductions in HR max with significant increases in $\dot{V}O_2$ max and $\dot{V}E$ max for all three groups.

Post2-Post1 comparisons revealed significant increases in HR max in all three groups. However, the response was much greater for the two beta blocked groups. $\dot{V}O_2$ max was significantly increased by 3.2 ml·kg·min^{-1} in the PR group and was unchanged in the PL and AT group. $\dot{V}E$ max was significantly increased in the PR and AT groups following the cessation of medication while no significant change was noted in the PL group. Here again, the magnitude of change was greatest for the PR group but this was expected due to the B_2 properties of this drug. These results indicate that the PR group did not realize its full training benefits until after cessation of the drug.

RPE Responses

The differentiated responses of RPE to acute beta blockade (Pre-C2) and the changes subsequent to 15 weeks of exercise endurance training for the four relative intensities of submaximal exercise, are presented in Tables 3 through 6. The submaximal RPE values obtained at that work intensity most closely approximating 60, 70, 80 and 90% of $\dot{V}O_2$ max were used in all subsequent analyses.

Acute beta blockade (Pre-C2) had little or no systematic effect on RPE at any of the relative intensities. At 60% of $\dot{V}O_2$ max, local RPE was significantly decreased by 1.1 and 1.2 scale units for the PL and PR groups respectively, central RPE was significantly decreased by 0.8 scale units in the AT group and overall RPE was significantly decreased by 0.8 and 0.7 scale units in the PL and AT groups respectively. At 90% of $\dot{V}O_2$ max, local RPE was significantly decreased by 0.7 scale units in the PL group and overall RPE was significantly decreased by 0.7 scale units in the AT group. However, the change in overall RPE at 90% $\dot{V}O_2$ was significantly different for the PR group, i.e. PR caused an increase in the overall RPE by 0.4 scale units, while overall RPE was decreased in both the PL and AT groups by 0.7 scale units.

Although the acute effect of beta blockade on the differentiated RPE responses were small, close inspection of Tables 3 through 6 demonstrate that the PR group had a

Table 3. Alterations in RPE subsequent to 15 weeks of Exercise Endurance Training at 60% $\dot{V}O_2$ max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
RPE Local								
Placebo	13.0±1.8	11.9±1.9[a]	9.6±1.6[b]	9.2±1.2[a]	-1.1	-2.3	-3.8	-0.4
Propranolol	13.6±1.8	12.4±1.3[a]	11.0±1.4[b]	10.6±1.8[a]	-1.2	-1.4[x,z]	-3.0	-0.4
Atenolol	12.9±2.0	12.4±1.8	9.3±1.5[b]	9.0±1.2[a]	-0.5	-3.1	-3.9	-0.3
RPE Central								
Placebo	11.6±1.4	11.1±1.7	9.3±1.4[b]	8.8±1.3[a]	-0.5	-1.8	-2.8	-0.5
Propranolol	12.2±1.8	12.0±2.1	10.7±1.3[b]	9.9±1.8[a,c]	-0.2	-1.3	-2.3	-0.8
Atenolol	11.7±1.5	10.9±1.4[a]	8.9±1.3[b]	8.6±1.1[a]	-0.8	-2.0	-3.1	-0.3
RPE Overall								
Placebo	12.1±1.5	11.3±1.5[a]	9.3±1.4[b]	8.9±1.3[a]	-0.8	-2.0	-3.2	-0.4
Propranolol	12.8±1.6	12.2±2.0	10.8±1.3[b]	10.1±1.6[a,c]	-0.6	-1.4	-2.7	-0.7
Atenolol	12.1±1.6	11.4±1.3[a]	9.1±1.4[b]	8.7±1.1[a]	-0.7	-2.3	-3.4	-0.4

a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1

x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

Table 4. Alterations in RPE subsequent to 15 weeks of Exercise Endurance Training, 70% $\dot{V}O_2$ max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
RPE Local								
Placebo	13.8±1.6	13.5±1.5	11.4±1.4[b]	11.0±1.9[a]	-0.3	-2.1	-2.8	-0.4
Propranolol	13.9±1.9	14.4±2.0	12.7±2.3[b]	12.1±2.0[a]	0.5	-1.7	-1.8	-0.6
Atenolol	13.4±2.3	13.4±2.4	10.7±2.0[b]	10.9±1.8[a]	0.0	-2.7	-2.5	0.2
RPE Central								
Placebo	12.9±1.6	12.9±1.7	11.5±1.8[b]	10.7±2.0[a]	0.0	-1.4	-2.2	-0.8
Propranolol	13.1±1.9	13.7±2.6	12.5±2.6[b]	11.4±2.1[a,c]	0.6	-1.2	-1.7	-1.1
Atenolol	12.5±2.2	12.5±1.9	10.7±2.3[b]	10.7±1.8[a]	0.0	1.8	-1.8	0.0
RPE Overall								
Placebo	13.3±1.7	13.0±1.5	11.4±1.6[b]	10.7±1.9[a]	-0.3	-1.6	-2.6	-0.7
Propranolol	13.5±2.0	13.9±2.4	12.4±2.5[b]	11.5±2.1[a,c]	0.4	-1.5	-2.0	-0.9
Atenolol	12.9±1.9	12.8±1.9	10.8±2.2[b]	10.7±1.9[a]	-0.1	-2.0	-2.2	-0.1

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

Table 5. Alterations in RPE subsequent to 15 weeks of Exercise Endurance Training, 80% $\dot{V}O_2$ max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
RPE Local								
Placebo	15.8±1.8	15.0±1.2	12.6±1.6[b]	12.9±1.4[a]	-0.8	-2.3	-2.9	-0.2
Propranolol	16.4±1.6	16.3±2.4	14.5±2.4[b]	13.3±2.5[a,c]	-0.1	-1.8	-3.1	-1.2[x,z]
Atenolol	15.8±1.9	15.5±2.4	12.9±1.7[b]	13.0±1.6[a]	-0.3	-2.6	-2.8	-0.1
RPE Central								
Placebo	14.7±1.4	14.5±1.8	12.3±1.4[b]	12.1±1.4[a]	-0.2	-2.2	-2.6	-0.2
Propranolol	15.3±1.8	15.5±2.7	14.1±2.8[b]	12.7±2.2[a,c]	0.2	-1.4	-2.6	-1.4[z]
Atenolol	14.8±2.0	14.5±2.4	12.2±2.1[b]	12.3±2.1[a]	-0.3	-2.3	-2.5	0.1
RPE Overall								
Placebo	15.2±1.4	14.7±1.5	12.5±1.1[b]	12.3±1.3[a]	-0.5	-2.2	-2.9	-0.2
Propranolol	15.7±1.8	15.9±2.6	14.0±2.7[b]	12.9±2.2[a,c]	0.2	-1.9	-2.8	-1.1
Atenolol	15.5±1.6	14.9±2.4	12.7±2.0[b]	12.7±1.7[a]	-0.6	-2.2	-2.8	0.0[y]

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

Table 6. Alterations in RPE subsequent to 15 weeks of Exercise Endurance Training, 90% of $\dot{V}O_2$ max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
RPE Local								
Placebo	17.6±1.4	16.9±1.7[a]	14.4±1.1[b]	14.4±1.5[a]	-0.0	-2.5	-3.2	0.0
Propranolol	18.3±1.3	18.2±1.9	16.0±2.2[b]	15.3±2.2[a,c]	-0.1	-2.2	-3.0	-0.7
Atenolol	18.1±1.4	17.5±2.1	15.3±1.9[b]	14.7±1.9[a,c]	-0.6	-2.2	-3.4	-0.6
RPE Central								
Placebo	16.9±1.7	16.5±1.6	14.0±1.4[b]	13.7±1.6[a]	-0.4	-2.5	-3.2	-0.3
Propranolol	17.4±1.7	17.7±2.5	15.4±2.4[b]	14.4±2.2[a,c]	0.3	-2.3	-3.0	-1.0
Atenolol	18.0±1.5	16.8±2.3	14.8±2.5[b]	13.9±2.5[a,c]	-1.2	-2.0	-4.1	-0.9
RPE Overall								
Placebo	17.3±1.4	16.6±1.6	14.1±1.2[b]	13.8±1.6[a]	-0.7	-2.5	-3.5	-0.3
Propranolol	17.7±1.7	18.1±2.1	15.7±2.3[b]	14.7±2.1[a,c]	0.4[x,z]	-2.4	-3.0	-1.0
Atenolol	18.0±1.5	17.3±2.1[a]	15.1±2.3[b]	14.6±2.1[a]	-0.7	-2.2	-3.4	-0.5

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

tendency to rate the work performed at each relative intensity higher than either the PL or AT groups, indicating that the PR group perceived the work to be harder than the other groups.

The Post1-Pre comparisons were consistent throughout each relative intensity, i.e. all three RPE ratings were significantly decreased in each group at all relative intensities, thus indicating that a training effect had taken place even while under the influence of beta blockade. Again, the PR group consistently rated each relative intensity higher than either the PL or AT groups. Local RPE was significantly decreased by an average computed across the four relative intensities of -2.3, -1.8 and -2.7 scale units for the PL, PR and AT groups respectively. Central RPE was significantly decreased by -2.0, -1.6 and -2.0 scale units for the PL, PR and AT groups respectively. Overall RPE was significantly decreased by -2.1, -1.8 and -2.2 scale units for the PL, PR and AT groups respectively. In each of the differentiated ratings, the magnitude of the reduction in RPE was less for the PR group. This trend is consistent throughout the 70, 80 and 90% of $\dot{V}O_2$ max Post1-Pre comparisons, although statistical significance was not achieved.

The Post2-C2 comparison was also consistent throughout each relative intensity, i.e. RPE was significantly decreased. Local RPE was significantly decreased by

an average computed across the four relative intensities of -3.2, -2.7 and -3.2 scale units for the PL, PR and AT groups respectively. Central RPE was significantly decreased by -2.7, -2.4 and -2.9 scale units for the PL, PR and AT groups respectively. Overall RPE was significantly decreased by -3.1, -2.6 and -3.0 scale units for the PL, PR and AT groups respectively. Again, the magnitude of change was consistently smaller for the PR group for each of the three ratings, but there were no statistically significant differences in the magnitude of change between the two beta blocking drugs.

A most interesting result occurred in the Post2-Post1 comparison. At 60 and 70% of $\dot{V}O_2$ max, the PR group realized a significant decrease in both their central and overall RPE one week after drug cessation, a finding which should be independent of their training response. This phenomena occurred again at 80 and 90% of $\dot{V}O_2$ max for each of the three differentiated ratings. The AT group also realized a significant decrease in their local and central RPE at 90% $\dot{V}O_2$ max. This finding, at least for the PR group, indicates that this group perceived the same intensity of work as being more strenuous while they were medicated.

Local RPE was consistently rated higher than either central or overall RPE, and overall RPE was consistently rated higher than central RPE. When local and central RPE

values were averaged, the difference between the average value and the overall RPE never exceeded 0.2 scale units. Thus, the subjects were able to differentiate and integrate their RPE accurately. Since overall RPE represents a total integration of local and central sensations, it was used for the descriptive comparisons with the physiological variables of HR, $\dot{V}O_2$ and $\dot{V}E$.

RPE and Relative Stress Responses

Since RPE has been described as an index of the relative physiological stress associated with a given intensity of exercise, a regression analysis was conducted to predict the percentage of HR max, percentage of $\dot{V}O_2$ max, and percentage of $\dot{V}E$ max equivalent to RPE ratings (overall) of from 7.0 to 19.0 scale units (Tables 7-9).

Percentage of HR max

The PL group demonstrated a trend of accurate reproducibility of RPE when expressed as a percentage of HR max both before and after training, i.e. a rating of 13 occurred at 84.6, 84.0, 84.4 and 84.9% of HR max for the C2, Pre, Post1 and Post2 conditions respectively. However, beta blockade produced a somewhat different response. When blocked, both the PR and AT groups gave the same RPE value at a lower percentage of HR max. After training, for both Post1 and Post2 conditions, the same rating was associated with the same or a slightly higher percentage of HR max as

Table 7. RPE and relative stress responses to training and beta blockade.

Percentage HR max

	PL				PR				AT			
RPE	C2	Pre	Post1	Post2	C2	Pre	Post1	Post2	C2	Pre	Post1	Post2
7	65.3	60.6	59.9	59.8	62.9	60.6	57.5	57.6	67.1	56.6	59.5	62.8
8	68.5	65.8	64.0	64.0	66.2	63.7	61.2	61.9	69.9	60.2	62.6	66.3
9	71.7	69.4	68.1	68.2	69.4	66.9	65.0	66.1	72.6	63.8	65.7	69.9
10	74.9	73.1	72.2	72.3	72.6	70.0	68.7	70.3	75.3	67.4	68.8	73.4
11	78.2	76.7	76.2	76.5	75.8	73.2	72.5	74.5	78.1	71.0	71.9	77.0
12	81.4	80.4	80.3	80.7	79.1	76.3	76.2	78.7	80.8	74.5	75.0	80.5
13	84.6	84.0	84.4	84.9	82.3	79.5	80.0	82.9	83.6	78.1	78.1	84.0
14	87.8	87.6	88.5	89.1	85.5	82.6	83.7	87.1	86.3	81.7	81.2	87.6
15	91.0	91.3	92.6	93.2	88.7	85.8	87.5	91.3	89.0	85.3	84.3	91.1
16	94.2	94.9	96.7	97.4	92.0	89.0	91.2	95.5	91.8	88.9	87.4	94.7
17	97.4	98.6	100.8	101.6	95.2	92.1	95.0	99.7	94.5	92.4	90.5	98.2
18	100.6	102.2	104.9	105.8	98.4	95.3	98.7	104.0	97.3	96.0	93.6	101.8
19	103.8	105.9	109.0	110.0	101.7	98.4	102.5	108.2	100.0	99.6	96.7	105.3

Table 8. RPE and relative stress responses to training and beta blockade.

Percentage of $\dot{V}O_2$ max

	PL				PR				AT			
RPE	C2	Pre	Post1	Post2	C2	Pre	Post1	Post2	C2	Pre	Post1	Post2
7	36.2	37.4	40.3	42.8	36.2	40.7	36.1	36.1	42.5	39.4	43.7	44.4
8	41.5	42.7	45.4	47.6	41.5	45.5	41.4	41.6	47.0	44.5	47.9	48.6
9	46.8	48.1	50.5	52.5	46.7	50.3	46.8	47.1	51.6	49.5	52.2	52.9
10	52.0	53.4	55.6	57.3	51.9	55.1	52.2	52.5	56.1	54.6	56.4	57.2
11	57.3	58.8	60.8	62.2	57.2	59.9	57.5	58.0	60.6	59.7	60.6	61.4
12	62.6	64.1	65.9	67.0	62.4	64.7	62.9	63.4	65.1	64.8	64.8	65.7
13	67.9	69.5	71.0	71.9	67.6	69.5	68.3	68.9	69.7	69.8	69.0	70.0
14	73.1	74.8	76.1	76.7	72.9	74.3	73.6	74.4	74.2	74.9	73.3	74.3
15	78.4	80.2	81.2	81.5	78.1	79.1	79.0	79.8	78.7	80.0	77.5	78.5
16	83.7	85.6	86.3	86.4	83.3	83.9	84.4	85.3	83.2	85.1	81.7	82.8
17	89.0	90.9	91.5	91.2	88.6	88.7	89.7	90.8	87.7	90.2	85.9	87.1
18	94.3	96.2	96.6	96.1	93.8	93.5	95.1	96.2	92.3	95.2	90.2	91.4
19	99.5	101.6	101.7	100.9	99.0	98.3	100.5	101.7	96.8	100.3	94.4	95.6

Table 9. RPE and relative stress responses to training and beta blockade.

Percentage of $\dot{V}E$ max

	PL				PR				AT			
RPE	C2	Pre	Post1	Post2	C2	Pre	Post1	Post2	C2	Pre	Post1	Post2
7	3.3	10.7	20.7	23.0	-1.0	5.0	13.5	16.0	4.9	8.8	23.0	24.7
8	10.3	16.8	25.4	27.3	6.5	12.3	19.4	21.4	11.4	15.5	27.5	28.6
9	17.2	23.0	30.2	31.5	14.0	19.5	25.3	26.7	17.9	22.3	32.1	32.6
10	24.2	29.1	35.0	35.8	21.4	26.8	31.2	32.0	24.4	29.9	36.7	36.5
11	31.2	35.2	39.8	40.0	28.9	34.0	37.1	37.4	31.0	35.7	41.3	40.5
12	38.2	41.4	44.5	44.4	36.3	41.3	43.0	42.7	37.5	42.4	45.8	44.4
13	45.2	47.5	49.3	48.6	43.8	48.5	48.9	48.1	44.0	49.2	50.4	48.4
14	52.2	53.7	54.1	52.8	51.3	55.8	54.8	53.4	50.5	55.9	55.0	52.4
15	59.2	59.8	58.9	57.1	58.7	63.0	60.7	58.8	57.0	62.6	59.6	56.3
16	66.2	66.0	63.6	61.3	66.2	70.2	66.6	64.1	63.5	69.3	64.2	60.3
17	73.1	72.1	68.4	65.6	73.6	77.5	72.5	69.4	70.0	76.1	68.7	64.2
18	80.1	78.2	73.2	69.8	81.1	84.7	78.4	74.8	76.5	82.8	73.3	68.2
19	87.1	84.4	78.0	74.1	88.5	92.0	84.3	80.1	83.0	89.5	77.9	72.1

compared to C2 conditions. However, this result was not unexpected as it demonstrated that blocked individuals perceive the same relative work as being more stressful.

Percentage of $\dot{V}O_2$ max

All subjects, whether blocked or unblocked, trained or untrained, were able to reproduce any given RPE at the same percentage of $\dot{V}O_2$ max. This result in itself, demonstrates that RPE can be used as an accurate monitor of the relative exercise intensity.

Percentage of $\dot{V}E$ max

The PL group demonstrated agreement between C2 and Pre, i.e. the same RPE was associated with the same percentage of $\dot{V}E$ max. However, after training the same RPE was associated with a lower percentage of $\dot{V}E$ max. This is simply due to the fact that for the same submaximal level, $\dot{V}E$ will decrease while $\dot{V}E$ max increases; thus the ratio of submaximal $\dot{V}E$ to $\dot{V}E$ max will decrease. When blocked, both the PR and AT groups rated the same intensity of exercise with the same RPE, but due to a decrease in $\dot{V}E$ max this resulted in an increased percentage of $\dot{V}E$ max. After training, the PR and AT groups both decreased the percentage of $\dot{V}E$ max for any given RPE value while still blocked, with further decreases post-training and post-medication. This again demonstrates that the blocked individual perceives the same intensity of exercise as being more stressful.

CHAPTER 5

DISCUSSION

This chapter provides an analysis of the results, their implications, comparisons with previous research and an overview of the significance of this study.

Effect of Acute Beta Blockade on Resting, Submaximal and Maximal Responses

The acute effects of beta blockade on resting HR (Appendix E) are in agreement with the literature, i.e. a decreased HR (40, 47, 51, 54, 56-58, 120). The acute effect of beta blockade on submaximal HR was appropriate (25-30% reduction) for the level of blockade attained and consistent with other investigators (2, 3, 43-57). Maximal heart rate was reduced equally in both blocked groups, i.e. 44 and 49 beats·min^{-1} and the magnitude of the reduction in HR max is in agreement with the literature (2, 3, 43-57).

Submaximal oxygen uptake (Appendix F-J) was unchanged for the PL and PR groups, a finding which is consistent with most previous studies (2, 3, 40, 50, 55, 56). However, the AT group experienced a significant decrease in VO_2 following beta blockade at 60, 70 and 80% of VO_2 max, with no change at 90% of VO_2 max. This response, at the lower relative intensities with AT, agrees with Pearson, et

al. (51) who noted a 3.5% reduction in oxygen uptake over a range of submaximal workloads, and Reybrouck, et al. (54) who noted a 6% reduction at low levels of exercise, but not at higher levels. However, the acute maximal response ($\dot{V}O_2$ max) following beta blockade did not change in any of the three groups, a finding which is consistent with some studies (40, 56, 57), but in disagreement with others (51, 129).

Submaximal $\dot{V}E$ was unchanged for the PL group, but was significantly decreased for both blocked groups at 60% $\dot{V}O_2$ max, and significantly reduced in all three groups at 70% $\dot{V}O_2$ max. The only clear trend for relative intensities of 80 and 90% of $\dot{V}O_2$ max was a decrease in submaximal $\dot{V}E$ for the AT group, which may be associated with the decrease that was seen in the submaximal $\dot{V}O_2$ for that group. $\dot{V}E$ max was observed to decrease in both of the blocked groups, a finding which has been reported by others (40, 56).

Effect of Beta Blockade on Resting, Submaximal and Maximal Training Responses

Training studies on normal, healthy individuals who are placed on beta-blockade are seriously lacking and the literature is equivocal as to their findings (2-4). Other studies (5-11) have examined the trainability of cardiac patients and have reported generally favorable results. However, comparisons of normal with diseased populations could be misleading and therefore will not be discussed.

The resting HR response to training while blocked differs somewhat from other studies (2, 3). HR at rest decreased significantly by -6.5 beats·min^{-1} in the PR group, but no changes were found in the AT or PL group. Sable, et al. (2) and Marsh, et al. (3) found no change in resting HR in their PR group. The finding of no change in HR rest associated with training is generally inconsistent with the research literature. After drug cessation, HR increased significantly to near its initial level in both PR and AT groups. Sable et al. (2) reported a significant increase in HR to near initial levels, which is in agreement with this study, but Marsh, et al. (3) reported that HR increased, but not significantly, following cessation of medication.

Submaximal data are seldom reported in studies of training in normals under beta-blockade, with only Marsh et al. (3) reporting a decrease in submaximal HR of -15 beats·min^{-1} at approximately 52% of $\dot{V}O_2$ max. Generally, the reduction in HR for the same submaximal level of exercise is considered to be a classic response to endurance exercise training (22).

Maximal HR in this study significantly decreased in both blocked groups as well as in the placebo group consequent to training, but only in the unblocked post-training tests. A reduction in HR max consequent to training is consistent with the conclusions of Pollock (150), but is in

disagreement with Ewy, et al. (4) who reported an increase in HR max, and Sable, et al. (2) and Marsh, et al. (3) who reported no change in HR max following endurance training. After drug cessation, HR max significantly increased which is in agreement with the literature (2-4).

$\dot{V}O_2$ max, while blocked, was significantly increased in both groups following training, but the magnitude of the change was significantly less for the PR group (PL=+8.4, PR=+5.3, AT=+7.9, $ml \cdot kg^{-1} \cdot min^{-1}$). This is in agreement with Ewy, et al. (4) but in disagreement with two studies (2, 3) that have reported no change in $\dot{V}O_2$ max. The unblocked training response also demonstrated an increased $\dot{V}O_2$ max (PL=+7.9 PR=+7.2, AT=+7.6 $ml \cdot kg^{-1} \cdot min^{-1}$). The improvements noted in $\dot{V}O_2$ max were not significantly different between groups, thus all groups increased their $\dot{V}O_2$ max equally. After drug cessation, $\dot{V}O_2$ max significantly increased by +3.2 $ml \cdot kg^{-1} \cdot min^{-1}$ for the PR group, but did not change in either the PL or AT groups. Propranolol appears to mask the improvements in endurace capacity while still under treatment with the drug. Both Sable, et al. (2) and Marsh, et al. (3) reported no change in $\dot{V}O_2$ max for their beta blocked subjects post-training, either while on or off of the drug. The magnitude of improvement reported by Ewy, et al. (4) for their sotalol group was of a lower magnitude (+3.2 $ml \cdot kg^{-1} \cdot min^{-1}$) than that reported in the present study.

$\dot{V}E$ max, while blocked, significantly increased post-training. This is in agreement with Sable, et al. (2) but disagrees with others (3, 4) who found no change. In the unblocked state, all groups realized a training increase in $\dot{V}E$ max, which is in agreement with two of the previous studies using beta blockers (2, 4). After drug cessation, $\dot{V}E$ max significantly increased for both the PR and the AT groups but the magnitude of the change was significantly greater for the PR group (PR=+20.5, AT=11.1 liters$\cdot$min^{-1}).

Submaximal RPE Responses to Beta Blockade and Training

Several investigators have examined the acute RPE response to beta blockade both in healthy individuals (51, 58, 67, 86, 118, 125, 126, 129) and in diseased populations (127, 128). In each case, except for the study by Pearson, et al. (51), beta blockade substantially reduced the HR, yet, there was no change in RPE, a finding consistent with the present study. Pearson, et al. (51) reported an increase of 0.73 scale units at the same absolute workloads following beta blockade.

The present study reported three differentiated ratings of perceived exertion, i.e. local, central, and overall RPE, while the majority of studies have only reported an overall RPE rating. One study (129) reported both a local and a central RPE but did not report an overall rating. These differences in protocol make comparisons

difficult. In the investigation by Tesch and Kaiser (129) the local RPE was rated higher than the central RPE both before and after beta blockade in both submaximal and maximal exercise. In addition, during maximal exercise, there was no change in either RPE rating following beta blockade. During submaximal exercise, there was a significant increase in the local rating when blocked (+1.6 scale units), but not in the central rating, a finding which tends to be in partial agreement with Pearson, et al. (51).

Local RPE was consistently rated higher than either central or overall RPE and overall RPE was consistently rated higher than central RPE. This is in agreement with Tesch and Kaiser (129). The PR group also consistently rated each of the three ratings higher than either the PL or AT groups, thus indicating that the PR group perceived the same intensity of work to be more difficult than that perceived by either the PL or AT group. However, unlike Pearson, et al. (51) and Tesch and Kaiser (129), all ratings in this study tended toward either no change or a slight decrease in RPE.

The effect of training, while blocked, on RPE has not been previously reported in the literature. For each of the three ratings, and at all relative intensities for and each group, this study demonstrated a highly significant decrease in RPE as a result of endurance training, but the magnitude of this decrease was least for the PR group.

This indicates that a substantial training effect occurred, but this effect was not as pronounced in the PR group, at least while they were blocked.

The submaximal RPE response to training, in the unblocked state, was similar to the blocked state, i.e. all RPE ratings for all drug groups significantly and substantially decreased, further substantiating a training effect. However, when the RPE responses were equated in terms of relative intensity (% $\dot{V}O_2$ max - Table 8), there were no differences in RPE, pre- or post-training, blocked or unblocked, for either the PR or AT groups. This finding is in agreement with earlier investigations by Ekblom and Goldbarg (86) and Docktor and Sharkey (95) who observed that the training induced decrement in submaximal heart rate would correspond to a subsequent reduction in RPE. Ekblom and Goldbarg (86) further observed that this reduced RPE would actually be unchanged if expressed in terms of relative heart rate or oxygen consumption, a finding confirmed in the present study (Tables 7 and 8). However, there was a tendency to rate the work higher while blocked, when RPE was expressed both as a percentage of HR max and $\dot{V}E$ max. This suggests that HR is not a primary cue in the perception process. This, however, does not imply that central mechanisms should be overlooked in assessing the total sensory process of perception.

After drug cessation, RPE did not significantly change for either the PL or AT groups (except at 90% VO_2 max for AT where significant decreases in local and central ratings were noted), but there was a tendency toward a decrease in ratings. However, the PR group (except for the local RPE at 60 and 70% of $\dot{V}O_2$ max) demonstrated a significant decrease in all ratings. This finding again indicates that in terms of absolute workloads, the PR group perceived their work to be more difficult while blocked.

Significance of the Results

This study has clearly demonstrated that healthy, normal but untrained, beta-blocked individuals can obtain a trained state, and that the magnitude of their physiological changes will be similar to those of unblocked individuals who are subjected to exercise endurance training. Even in the presence of beta blockade, $\dot{V}O_2$ max, $\dot{V}E$ max, and HR max will respond in a typical manner. This study has also demonstrated that the non-selective beta blocker propranolol may potentially "mask" these results, where the more cardioselective beta blocker atenolol allows a response similar to that of a placebo. Of possible importance to the interpretation of this study is the length, mode and intensity of the training program. These factors must be taken into consideration since studies of shorter length and lower intensity have not been able to demonstrate a training response.

This study further demonstrated that RPE is not affected by beta blockade. This suggests that HR, which is attenuated by beta blockade, is not a primary sensory cue in the perception of exertion. Also demonstrated was the consistently higher rating of the local RPE, indicating that either or both metabolic and cardiovascular changes in the exercising muscle may play a primary role in the perception of exertion. RPE at the same absolute workloads will decrease significantly as a result of training, but when expressed in relative terms, RPE will not change. This finding indicates that RPE is a reliable indicator of the relative physiological stress and can be used as a safe monitor of the relative exercise intensity, at least in the population studied.

CHAPTER 6

SUMMARY AND CONCLUSIONS

This chapter provides a brief review of the purpose, design and results of this study. A summary of the major conclusions based on these results is also included.

Summary

Forty-seven out of an original population of 52 college age (17-34 years) males were randomly assigned to one of three groups: placebo, propranolol (160 mg/day) or atenolol (100 mg/day), in order to study the effect of beta adrenergic blocking agents on the ability to obtain a trained exercise state and on the individual's ratings of perceived exertion.

Following the administration of an extensive physical examination, the subjects participated in five different treadmill testing sessions. The first test was a standard maximal exercise test with speed held constant at 3.5 mph (5.64 km/hr) and grade increased by 3% every two minutes up to the point of volitional fatigue. A treadmill grade equivalent to 60% VO_2 max was then determined individually for each subject by linear regression of

treadmill grade and oxygen uptake. This grade was then used to obtain steady state submaximal measurements during the subsequent testing sessions. The second through fifth tests were identical in protocol, and included both a submaximal, steady-state period and a graded test to exhaustion. The first and second tests were used to establish test reliability during maximal exercise (Table 2). Having established excellent reliability, Control test 2 was then used for all subsequent comparisons. Following the second test the subjects were randomly assigned to one of the treatment groups on a double blind basis. One week later a third exercise test was conducted to determine the acute effects of beta blockade. At this point, the subjects began the monitored exercise training sessions.

Training was conducted at a THR of 70-85% of $\dot{V}O_2$ max. All sessions began with a warmup period. Subjects initially walked/jogged for 30 minutes until at the end of the 15 weeks of training they were able to run continuously for 45 minutes. Compliance was high, with each group completing 96.7 to 98.2% of the 75 monitored exercise sessions.

During the fourteenth week of training a fourth test was conducted to establish the training effects, if any, that had taken place while the subjects were still medicated. Following this test, medication was stopped and the subjects continued to train for one additional week.

After fifteen weeks of training a fifth and final test was conducted to establish the training effects, if any, which had been achieved as a result of training itself.

The results of this study indicate that all of the subjects obtained a training effect, regardless of the medication they received. This was evidenced by significant increases in $\dot{V}O_2$ max, $\dot{V}E$ max, and a significant decrease in HR max. It is important to note that the magnitude of these changes in the PR group were either lower or they were "masked" until the effects of the drug were no longer evident. At submaximal levels of exercise, VE and HR significantly decreased, while $\dot{V}O_2$ was not significantly altered in any group. These effects were noted whether the subject was blocked or unblocked post-training.

Differentiated ratings of perceived exertion during submaximal levels of exercise at the same absolute work rate were observed to significantly decrease with training, both blocked and unblocked. This also was evidence of a classic response to training. However, RPE for the same relative percentage of $\dot{V}O_2$ max was unchanged. A "masking" effect was evident in the propranolol group, indicating that they perceived the work to be more difficult than what was perceived by either the atenolol or placebo group. Furthermore, local RPE was observed to be greater than central or overall RPE and overall RPE was consistently greater than central RPE. Acute beta blockade did not

alter RPE for the same level of exercise, thus suggesting that HR is not a major determinant of perception and that local metabolites in the exercising muscle may play a more dominant role. Also, these results substantiate RPE as a viable index of exercise intensity for purposes of prescribing exercise.

Conclusions

1. Normal, sedentary subjects who undertake a rigorous endurance training program while under the influence of beta blockade will obtain the same classical physiological responses to exercise endurance training as those of similar but unblocked individuals.
2. These responses may be "masked" while the individual is blocked and therefore, an adequate period of time should pass after drug cessation before any post-training tests are conducted.
3. The duration, frequency and intensity of the training program appear to be critical to the magnitude of the blocked individual's response to training.
4. Submaximal RPE for the same intensity of exercise decreases as a result of training. However, when expressed in relative terms, RPE does not change.
5. For the population studied, RPE is an effective monitor of the relative exercise intensity.
6. RPE does track HR when influenced by beta blockade as the slopes of the lines are the same. However, the

intercepts are different and may indicate that HR is not a primary sensory cue in the perception of exertion.

7. Local RPE is rated higher than either central or overall RPE. Therefore, local sensations from the exercising muscles are involved, in part, in the integration of sensory cues which result in the perception of effort.

APPENDIX A

SUBJECT'S CONSENT FORM

University of Arizona

Effect of Beta Blockade on Achievement of the Trained Exercise State

I understand that I am being asked to voluntarily participate in a study entitled, **Effect of Beta Blockade on Achievement of the Trained Exercise State.** The purpose of this investigation is to determine the influence of two beta adrenergic blocking drugs named atenolol and propranolol on the ability to gain the usual physiological benefits from an exercise training program. Beta blocking drugs produce effects within your body which include slowing of your heart rate and inhibiting the elevated blood pressure effects of "adrenalin," the hormone that we all release when we are frightened. The drug will be taken by mouth several times a day. Potential side effects from short-term or chronic use of this drug include mild gastrointestinal upset, nausea and fatigue.

Testing Phase

If I decide to participate, I will be given a comprehensive physical examination by a physician and blood will be drawn for screening blood chemistries. A standard electrocardiogram will also be performed. I will then complete two exercise tests to exhaustion on a motor driven treadmill, starting at a slow walk with an increase in speed and grade every two minutes until I decide that I cannot go any longer. A minimum of two days, but not more than seven days will intervene between the first two maximum tests. During this time, I will also undergo two determinations of my body composition by being weighed underwater ten times for each determination. I will exhale all of the air out of my lungs while totally submerged under water for a period of 5-10 seconds while seated in a chair suspended from a scale. Prior to each determination, I will perform two tests to determine my residual lung volume, which is the air remaining in my lungs following a maximal expiration. This will involve breathing into and out of a spirometer for a period of 5-10 seconds. I will also undergo the drawing of two blood samples (10 ml, or slightly more than two teaspoons, each) from which a determination will be made of the content of blood fat, and other routine examinations.

Following the initial tests, I will be given daily oral doses of a beta adrenergic blocking drug or a placebo (sugar pill). Following the first week on this drug/placebo, I will repeat the treadmill test to exhaustion.

During the course of the training program, I will undergo five additional blood draws, one each at the end of the 1st, 3rd, 6th, 12th, and 13th week (10 ml per sample, or slightly more than two teaspoons each), from which they will determine the concentration of the beta adrenergic blocking drug and blood chemistries.

At the 13th week, I will again undergo underwater weighing and a treadmill test to exhaustion. I will then discontinue the drug/placebo and will repeat the treadmill test one week following discontinuation of the drug/placebo. I will continue exercising during this final week.

During the treadmill test, I understand that exercise physiologists will be monitoring my blood pressure, heart rate, and electrocardiogram. In addition, they will be monitoring my energy expenditure through the amount of oxygen I consume. There is a very remote possibility that certain abnormal changes might occur during the treadmill test, including abnormal blood pressure or electrocardiogram responses. Every effort will be made to minimize the possibilities of these occurrences by close observation and monitoring of my performance during the test. Further, emergency equipment such as a defibrillator, drugs, etc. will be available, if necessary. During the blood draw, I realize there is the usual discomfort associated with the initial puncture of the skin with the needle. There is also the possibility of a hematoma (some blood leaking from the vein and collecting under the skin) causing local swelling associated with drawing blood samples.

Training Program

I will be participating in a fifteen-week training program, walking, jogging or running five days per week, for 45 minutes per day. My intensity of exercise will be monitored by my training heart rate, which has been established as that heart rate which corresponds to 75% of my maximal oxygen uptake ($\dot{V}O_2$ max) which is the physiological index of my endurance capacity. Each training session will be monitored by a trained exercise specialist. I understand that I will be instructed in the correct method of jogging, footwear requirements, avoidance of auto-pedestrian encounters and stress fracture avoidance.

Conditions of Participation

As a participant in this study, I will gain an understanding of my medical and physiological profile, both prior to and following a period of endurance training. I will also be in much better physical condition and will have a more favorable body composition. I am also aware that these findings may have significant implications for the future prescription of exercise in patients with coronary artery disease.

I understand that all information concerning my performance of the various tests associated with this study will be kept confidential, and all data will be filed according to a subject number identification code system. I realize that all procedures will be under the constant supervision of a physician and an exercise physiologist.

I also understand that this consent form will be filed in an area designated by the Human Subjects Committee, with access restricted to the principle investigators or authorized representatives of their particular departments.

I am also aware that in the event of injury resulting from any of the above stated procedures, I will receive no compensation for wages, lost time, medical expenses or hospitalization.

I understand tht my involvement in this study will not cost me any money. I will however, receive a total of $350 for completing all phases of this study. For patient populations, this money will be applied to the charges associated with my participation in the University of Arizona's Cardiorespiratory Rehabilitation Program.

I have read the above "Subject's Consent Form." The nature, demands, risks and benefits of the project have been explained to me. I understand that I may ask questions and that I am free to withdraw from the project at any time without ill will.

Subject's Signature _____ Date _____

Witness' Signature _____ Date _____

I have carefully explained to the subject the nature of the above project. I hereby certify that to the best of my knowledge, the subject signing this consent form understands clearly the nature, demands, benefits and risks involved in participating in this study. A medical problem, or language or educational barrier has not precluded a clear understanding of his/her involvement in this project.

A copy of this consent form is available to subjects on request.

Physician's Signature _____ Date _____

Witness' Signature _____ Date _____

APPENDIX B

THE UNIVERSITY OF ARIZONA
HEALTH SCIENCES CENTER
TUCSON, ARIZONA 85724

HUMAN SUBJECTS COMMITTEE
1609 N. WARREN (BUILDING 220), ROOM 112

TELEPHONE: (602) 626-6721 or 626-7575

27 December 1983

Jack H. Wilmore, Ph.D.
Department of Physical Education
Exercise and Sport Sciences Laboratory
MAIN CAMPUS

Dear Dr. Wilmore:

We are in receipt of your 20 December 1983 memoranda and the accompanying revised consent form for your project, "Effect of Beta Blockage on Achievement of the Trained Exercise State" (HSC #83-56). The changes outlined in these memoranda are minor and pose no further risk to the subjects involved. Therefore, approval for these changes is granted effective 27 December 1983.

The changes approved are:

1. Revision of the consent form to better explain the study's 15-week training period (no change in approved procedures involved).

2. Decrease in subject remuneration from $500 to $350.

3. Addition of Dr. Ron Watson as co-investigator.

4. Addition of a consent form addendum to allow for the collection of four 7 ml blood samples; two prior to exercise training and two following exercise training.

Approval is granted with the understanding that no further changes will be made in either the procedures followed or in the consent form to be used (copies of which we have on file) without the knowledge and approval of the Human Subjects Committee and the College or Departmental Review Committee. Any physical or psychological harm to any subject must also be reported to each committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely yours,

Milan Novak

Milan Novak, M.D., Ph.D.
Chairman
Human Subjects Committee

MN/jm

APPENDIX C

PROTOCOL

Time min	Speed mph	Grade %
0-1	3.5	0
1-2	3.5	0
2-3	3.5	3
3-4	3.5	3
4-5	3.5	6
5-6	3.5	6
6-7	3.5	9
7-8	3.5	12
8-9	3.5	12
9-10	3.5	12
10-11	3.5	15
11-12	3.5	15
12-13	3.5	18
13-14	3.5	18
14-15	3.5	21
15-16	3.5	21
16-17	3.5	24
17-18	3.5	24

APPENDIX D

THE BORG SCALE

6	
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very, very hard
20	

Appendix E. Alterations in Resting Heart Rate and Blood Pressure Consequent to 15 Weeks of Exercise Endurance Training

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
Systolic BP, mmHg								
Placebo	126.1± 6.9	127.7± 6.5	126.4± 8.3	127.5± 9.0	1.6	-1.3	1.4	1.1
Propranolol	126.5± 9.8	120.3± 8.8[a]	120.7± 9.7	125.9± 8.3[c]	-6.2[x]	0.4	-0.6	5.2[x]
Atenolol	129.9±11.5	120.6±10.2[a]	121.9± 9.0	130.6± 9.5[c]	-9.3[x]	1.3	0.7	8.7[x]
Diastolic BP, mmHG								
Placebo	74.4± 8.0	77.1± 7.4	76.7± 8.4	75.6± 9.7	2.7	-0.4	1.2	-1.1
Propranolol	80.3± 7.2	76.8± 6.0	73.7± 5.4[b]	76.7± 7.0	-3.5	-3.1	-3.6	3.0
Atenolol	79.2±15.2	76.2±13.3	73.5±16.8[b]	78.5± 6.4	-3.0	-2.7	-0.7	5.0
Heart Rate, beats·min^{-1}								
Placebo	69.5±10.7	65.3±11.0	63.7± 9.8	66.9±13.5	-4.2	-1.6	-2.6	3.2
Propranolol	68.9±10.2	57.6± 8.7[a]	51.1± 9.2[b]	68.6±13.0[c]	-11.3[x]	-6.5	-0.3	17.5[x]
Atenolol	68.8±11.1	53.7± 8.5[a]	50.1± 9.2	64.1±10.3[c]	-15.1[x]	-3.6	-4.7	14.0[x]

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1

x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

AD-A148 053 THE EFFECT OF BETA ADRENERGIC BLOCKADE ON RATINGS OF PERCEIVED EXERTION(U) AIR FORCE INST OF TECH WRIGHT-PATTERSON AFB OH A A HARTZELL 1984 2/2

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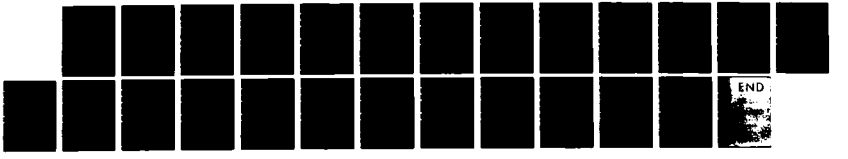

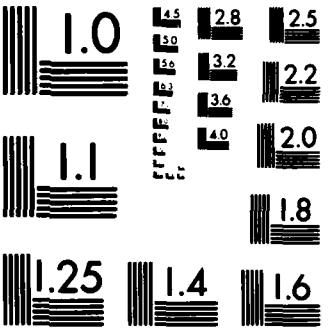

Appendix F. Metabolic and Cardiovascular Alterations Subsequent to 15 Weeks of Exercise Endurance Training at 60% $\dot{V}O_2$ max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
$\dot{V}O_2$, ml·kg^{-1}·min^{-1}								
Placebo	28.8 ± 3.4	28.2 ± 3.7	28.6 ± 3.2	27.7± 3.5[c]	-0.6	0.4	-1.1	-0.9
Propranolol	28.1 ± 5.8	27.6 ± 6.5	26.9 ± 5.7	26.7± 5.8	-0.5	-0.7	-1.4	-0.2
Atenolol	26.5 ± 4.5	25.3 ± 4.1[a]	25.8 ± 4.4	25.9± 4.3	-1.2	0.5[x]	-0.6	0.1[x]
$\dot{V}E$, liters·min^{-1}								
Placebo	60.0 ± 7.5	57.9 ± 7.9	55.2 ± 6.1[b]	54.6± 5.8	-2.1	-2.7	-5.4	-0.6
Propranolol	62.4 ± 7.6	58.6 ± 9.0[a]	54.3 ± 7.2[b]	56.1± 8.7[a]	-3.8	-4.3	-6.3	1.8
Atenolol	58.7 ±12.8	54.4 ± 9.9[a]	51.8 ± 9.7[b]	54.3± 11.1[c]	-4.3	-2.6	-4.4	2.5[x]
R								
Placebo	0.96± 0.04	0.96± 0.04	0.91± 0.04[b]	0.93± 0.04[a]	0.0	-0.06	-0.03	0.02
Propranolol	0.96± 0.05	0.96± 0.06	0.93± 0.03[b]	0.93± 0.04[a]	0.0	-0.03	-0.03	0.0
Atenolol	0.98± 0.04	0.98± 0.06	0.91± 0.04[b]	0.94± 0.05[a,c]	0.0	-0.07	-0.05	0.03[y]
Systolic BP, mmHg								
Placebo	169.0± 13.1	159.4± 15.1[a]	160.8 ± 7.9	156.3± 11.4[a]	-9.6	1.4	-12.7	-4.5
Propranolol	175.2± 16.6	146.9± 15.9[a]	140.6 ±12.4	157.8± 12.3[a,c]	-28.3[x]	-6.3	-17.4[z]	17.2[x,z]
Atenolol	175.2± 22.7	146.3± 16.0[a]	143.0 ±15.6	170.2± 19.6[c]	-28.9[x]	-3.3	-5.0	27.2[x,y]

Appendix F, Continued

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
Diastolic BP, mmHG								
Placebo	65.8±12.9	68.3± 9.3	66.9± 7.6	62.6±10.2	2.5	-1.4	-3.2	-4.3
Propranolol	70.3±15.1	69.3± 9.2	64.4± 8.5[b]	68.0± 7.0	-1.0	-4.9	-2.3	3.6[x]
Atenolol	71.1±12.2	69.9± 7.1	66.3± 8.3[b]	68.9± 8.2	-1.2	-3.6	-2.2	2.6[x]
Heart Rate, beats·min^{-1}								
Placebo	156.6±12.6	151.3±14.1	133.0±13.3[b]	130.6±11.4[a]	-5.3	-18.3[y,z]	-26.0	-2.4
Propranolol	158.2±12.7	115.8± 9.9[a]	105.0± 9.2	137.8±14.2[a,c]	-42.4[x]	-10.8	-20.4	32.8[x]
Atenolol	156.4±12.4	110.1± 8.7[a]	99.9± 9.3	133.2±10.9[a,c]	-46.3[x]	-10.2	-23.2	33.3[x]
$\dot{Q}$, liters·min^{-1}								
Placebo	14.2± 2.1	13.7± 1.9[a]	13.3± 2.0	12.8± 2.1[a,c]	-0.5	-0.4	-1.4	-0.5
Propranolol	13.3± 2.0	13.2± 2.2	12.0± 2.6[b]	12.2± 1.9[a]	-0.1	-1.2[x]	-1.1	0.2[x]
Atenolol	14.1± 2.5	13.6± 2.4[a]	12.7± 2.4[b]	13.6± 2.6[a,c]	-0.5	-0.9	-0.5	0.9[x]
SV, liters·min^{-1}								
Placebo	91.6±17.4	91.7±15.9	100.7±17.3[b]	98.7±16.6[a]	0.1[y,z]	9.0	7.1	-2.0
Propranolol	84.9±14.4	113.4±19.5[a]	112.0±20.1	89.1±14.0[c]	28.5	-1.4[x,z]	4.2	22.9[x]
Atenolol	90.3±16.4	119.6±20.6[a]	126.5±22.6[b]	102.3±20.3[a,c]	29.3	6.9	12.04	-24.2[x]

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

Appendix G. Metabolic and Cardiovascular Alterations Subsequent to 15 Weeks of Exercise Endurance Training at 70% $\dot{V}O_2$ Max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
$\dot{V}O_2$, $ml \cdot kg^{-1} \cdot min^{-1}$								
Placebo	32.3 ± 3.8	31.7 ± 3.8	32.7 ± 4.1	32.3 ± 3.6	-0.6	1.0	0.0	-0.4
Propranolol	30.2 ± 6.7	29.6 ± 7.6	29.4 ± 6.7	29.5 ± 7.0	-0.6	-0.2	-0.7	-0.1
Atenolol	29.4 ± 4.1	27.5 ± 4.0[a]	28.5 ± 3.9	28.9 ± 4.3	-1.9	1.0	-0.5	0.4
$\dot{V}E$, $liters \cdot min^{-1}$								
Placebo	68.8 ±10.0	66.2 ± 9.0[a]	62.6 ± 9.3[b]	63.3 ±10.2[a]	-2.6	-3.6	-5.5	0.7
Propranolol	67.9 ± 9.2	64.1 ±11.1[a]	60.6 ± 9.4[b]	60.6 ±11.1[a]	-3.8	-3.5	-7.3	0.0
Atenolol	66.1 ±10.5	61.9 ±10.1[a]	59.2 ± 7.6[b]	61.0 ±10.3[a]	-4.2	-2.7	-5.1	1.8
R								
Placebo	0.96± 0.03	0.96± 0.06	0.91± 0.05[b]	0.92± 0.06[a]	0.0	-0.05	-0.04	0.01
Propranolol	0.94± 0.05	0.96± 0.06	0.94± 0.04	0.93± 0.04	0.02	-0.02	-0.01	-0.01
Atenolol	0.96± 0.05	0.97± 0.05	0.91± 0.05[b]	0.93± 0.04[a]	0.01	-0.06	-0.03	0.02
Systolic BP, mmHg								
Placebo	168.7 ±11.6	165.5 ±14.5	167.8 ±13.7	167.3 ±12.6	-3.2	1.5	-1.4	0.3
Propranolol	174.8 ±18.7	149.1 ±18.7[a]	144.5 ±16.3	159.7 ±18.0[a,c]	-25.7[x]	-4.6	-15.1	15.2[x,z]
Atenolol	177.6 ±18.7	146.6 ±17.9[a]	144.1 ±17.8	173.7 ±16.2[c]	-31.0[x]	-2.5	-3.9	29.6[x,y]

Appendix G, Continued

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
Diastolic BP, mmHG								
Placebo	63.2±13.6	65.3±11.9	62.9± 9.6	59.7±13.8	2.1	-2.4	-3.5	-3.2
Propranolol	71.0±10.7	69.9± 8.8	63.9± 9.0[b]	67.2± 7.8	-2.0	-6.0	-4.7	3.3
Atenolol	70.0±11.6	69.9± 7.9	62.6±19.3[b]	64.4±10.0[a]	-0.1	-7.3	-5.6	1.8
Heart Rate, beats·min^{-1}								
Placebo	172.9±12.0	167.7±11.5	144.7±14.9[b]	143.7±12.5[a]	-5.2	-23	-29.2	-1.0
Propranolol	169.6±14.7	121.7± 9.8[a]	111.2±11.9[b]	149.0±18.9[a,c]	-47.9[x]	-10.5[x]	-20.6	37.8[x]
Atenolol	172.0±10.5	124.5±18.8[a]	108.3±10.0[b]	144.4±14.4[a,c]	-47.5[x]	-16.2	-27.6	36.1[x]

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

Appendix H. Metabolic and Cardiovascular Alterations Subsequent to 15 Weeks of Exercise Endurance Training at 80% VO_2 max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
$\dot{V}O_2$, $ml \cdot kg^{-1} \cdot min^{-1}$								
Placebo	36.0 ± 3.5	35.6 ± 3.3	37.4 ± 4.0[b]	36.6 ± 4.0	-0.4	1.8	0.6	-0.8
Propranolol	34.6 ± 7.3	34.0 ± 7.8	33.6 ± 7.1	34.0 ± 7.4	-0.6	-0.4[x]	-0.6	0.4
Atenolol	33.6 ± 4.8	32.4 ± 4.2[a]	32.8 ± 4.6	33.2 ± 4.7	-1.2	0.4[x]	-0.4	0.4
$\dot{V}E$, $liters \cdot min^{-1}$								
Placebo	85.2 ±11.8	81.5 ±10.9	76.3 ±11.2[b]	74.8 ±11.0[a]	-3.7	-5.2	-10.4	-1.5
Propranolol	84.9 ±13.3	81.0 ±14.8	72.6 ±12.8[b]	74.7 ±15.4[a]	-3.9	-8.4	-10.2	2.1
Atenolol	83.3 ± 9.2	79.0 ±13.4[a]	71.4 ± 9.5[b]	72.1 ±12.5[a]	-4.3	-7.6	-11.2	0.7
R								
Placebo	1.04± 0.04	1.03± 0.06	0.95± 0.04[b]	0.96± 0.05[a]	-0.01	-0.08	-0.08	0.01
Propranolol	1.01± 0.06	1.04± 0.07	0.99± 0.04[b]	0.98± 0.04	0.03	-0.05	-0.03	-0.01
Atenolol	1.04± 0.09	1.05± 0.08	0.97± 0.06[b]	0.97± 0.04[a]	0.01	-0.08	-0.07	0.0
Systolic BP, mmHg								
Placebo	175.9 ±11.9	171.3 ±14.7	175.7 ±13.0	175.1 ±14.2	-4.6	4.4	-0.8	-0.6
Propranolol	185.9 ±19.0	155.5 ±20.1[a]	151.9 ±15.7	171.5 ±16.5[a,c]	-30.4[x]	-3.6	-14.4[x,z]	19.6[x,z]
Atenolol	183.7 ±20.4	155.5 ±20.5[a]	151.8 ±18.6	184.5 ±17.6[c]	-28.2[x]	-3.7	0.8	32.7[x,y]

Appendix H, Continued

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
Diastolic BP, mmHG								
Placebo	62.0±14.3	63.1±10.7	62.5±11.4	58.3±12.6	1.1	-0.6	-3.7	-4.2
Propranolol	64.3±21.7	70.0± 7.6	62.8± 9.8[b]	66.4± 8.7	5.7	7.2[x]	2.1	3.6[x]
Atenolol	65.9±12.3	69.1± 8.2	62.4± 8.5[b]	62.9±12.2	3.2	-6.7[x]	-3.0	0.5
Heart Rate, beats·min^{-1}								
Placebo	182.7±11.0	181.1± 9.3	156.6±13.4[b]	157.7±12.7[a]	-1.6	-24.5	-25.0	1.1
Propranolol	181.1±12.3	132.6± 9.7[a]	119.6±12.1[b]	162.4±18.4[a,c]	-48.5[x]	-13.0[x]	-18.7	42.8[x]
Atenolol	182.1± 9.6	131.9±10.0[a]	116.7±10.5[b]	159.8±13.1[a,c]	-50.2[x]	-15.2[x]	-22.3	43.1[x]

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

Appendix I. Metabolic and Cardiovascular Alterations subsequent to 15 Weeks of Exercise Endurance Training at 90% $\dot{V}O_2$ max.

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
$\dot{V}O_2$, ml·kg^{-1}·min^{-1}								
Placebo	41.0 ± 4.1	40.6 ± 3.6	41.6 ± 4.6	40.3 ± 4.4[c]	-0.4	1.0	-0.7	-1.3
Propranolol	39.1 ± 7.8	39.0 ± 8.9	39.0 ± 7.7	38.9 ± 7.7	-0.1	0.0	-0.2	-0.1[x]
Atenolol	38.2 ± 5.1	37.4 ± 4.9	37.8 ± 4.4	38.3 ± 5.1	-0.8	0.4	0.1	0.5[x]
$\dot{V}E$, liters·min^{-1}								
Placebo	112.7 ±13.6	105.3 ±12.0[a]	92.2 ±12.6[b]	89.9 ±11.9[a]	-7.4	-13.1	-22.8	-2.3
Propranolol	112.7 ±19.8	110.3 ±19.0	94.0 ±18.6[b]	93.5 ±18.2[a]	-2.4	-16.3	-19.2	-0.5
Atenolol	113.7 ±17.7	107.0 ±16.2[a]	93.0 ±17.8[b]	92.9 ±14.8[a]	-6.7	-14.0	-20.8	-0.1
R								
Placebo	1.14± 0.04	1.12± 0.06	1.01± 0.04[b]	1.02± 0.06[a]	-0.02	-0.11	-0.12	0.01
Propranolol	1.11± 0.07	1.15± 0.09[a]	1.08± 0.05[b]	1.05± 0.04[a,c]	0.04[x]	-0.07	-0.06	-0.03[x]
Atenolol	1.16± 0.12	1.17± 0.10	1.06± 0.09[b]	1.04± 0.06[a]	0.01	-0.11	-0.12	-0.02
Systolic BP, mmHg								
Placebo	181.5 ±13.4	181.2 ±15.5	183.3 ±11.9	184.1 ±13.3	-0.3	2.1	2.6	0.8
Propranolol	194.4 ±17.3	164.5 ±19.9[a]	160.7 ±13.3	183.3 ±12.7[a,c]	-29.9[x]	-3.8	-11.1[x]	22.6[x]
Atenolol	192.7 ±22.7	170.1 ±20.5[a]	163.2 ±19.6	190.4 ±18.3[c]	-22.6[x]	-6.9	-2.3	27.2[x]

Appendix I, Continued

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
Diastolic BP, mmHG								
Placebo	62.0±13.6	62.1±12.5	60.7±13.4	56.7±14.7	0.1	-1.4	-5.3	-4.0
Propranolol	62.7±20.9	70.5± 8.4[a]	62.7±10.9[b]	63.1±10.1	7.8	-7.8	0.4	0.4
Atenolol	62.7±16.6	70.1± 9.0[a]	60.9±11.2[b]	60.5±19.5	7.4	-9.2[x]	-2.2	-0.4
Heart Rate, beats·min^{-1}								
Placebo	191.5± 8.1	189.2± 9.0	169.7±12.8[b]	169.7±11.1[a]	-2.3	-19.5	-21.8	0.0
Propranolol	191.9± 9.9	143.0±10.6[a]	131.6±12.1[b]	175.1±15.9[a,c]	-48.9[x]	-11.4[x]	-16.8	43.5[x]
Atenolol	192.4± 7.5	145.1±13.0[a]	128.1±12.7[b]	172.9±12.9[a,c]	-47.3[x]	-17.0	-19.5	44.8[x]

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

Appendix J. Maximal Metabolic and Cardiovascular Alterations Subsequent to 15 Weeks of Exercise Endurance Training

Variable	Control 2	Pre	Post 1	Post 2	Mean Differences			
					Pre-Con 2	Post 1-Pre	Post 2-Con 2	Post 2-Post 1
$\dot{V}O_2$, ml·kg^{-1}·min^{-1}								
Placebo	45.4 ± 4.5	45.6 ± 4.2	54.0 ± 3.1^{b}	53.3 ± 3.2^{a}	0.2	8.4^{y}	7.9	-0.7
Propranolol	42.4 ± 8.7	41.1 ± 8.3	46.4 ± 6.9^{b}	49.6 ± 8.1^{a,c}	-1.3	5.3	7.2	3.2^{x,z}
Atenolol	41.5 ± 5.6	40.7 ± 5.9	48.6 ± 6.9^{b}	49.1 ± 7.1^{a}	-0.8	7.9^{y}	7.6	0.5
$\dot{V}E$, liters·min^{-1}								
Placebo	146.7 ±21.8	146.5 ±26.4	163.9 ±21.6^{b}	168.8 ±19.5^{a}	-0.2	17.4	22.1	4.9
Propranolol	139.8 ±19.5	123.9 ±18.2^{a}	139.7 ±13.8^{b}	160.2 ±17.7^{a,c}	-15.9^{x}	15.8	20.4	20.5^{x,z}
Atenolol	145.7 ±19.6	133.6 ±17.7^{a}	151.3 ±14.1^{b}	162.4 ±15.8^{a,c}	-12.1^{x}	17.7	16.7	11.1
R								
Placebo	1.22± 0.07	1.22± 0.07	1.23± 0.07	1.21± 0.07	0.0	0.01	-0.01	-0.02
Propranolol	1.18± 0.05	1.19± 0.08	1.22± 0.04	1.23± 0.04	0.01	0.03	0.05	0.01
Atenolol	1.24± 0.11	1.25± 0.10	1.20± 0.07	1.23± 0.06	0.01	-0.05	-0.01	0.03
Treadmill Time, min								
Placebo	16.1 ± 1.7	16.6 ± 1.8^{c}	19.4 ± 1.2^{b}	19.9 ± 1.5^{a,c}	0.5	2.8	3.8	0.5
Propranolol	14.9 ± 3.4	14.1 ± 3.0^{a}	16.2 ± 2.6^{b}	18.0 ± 3.6^{a,c}	-0.8^{x,z}	2.1	3.1	1.8^{x,z}
Atenolol	14.5 ± 1.8	14.4 ± 2.1	17.0 ± 2.7^{b}	18.0 ± 2.6^{a,c}	-0.1	2.6	3.6	1.0
Heart Rate, beats·min^{-1}								
Placebo	197.0 ± 7.1	197.5 ± 5.2	189.7 ±10.7^{b}	192.1 ± 8.6^{a,c}	0.5	-7.8	-4.9	2.4
Propranolol	198.0 ± 7.8	149.4 ±12.6^{a}	144.6 ±10.4	195.2 ± 9.0^{a,c}	-48.6^{x}	-4.8	-2.8^{z}	50.6^{x,z}
Atenolol	199.7 ± 7.6	155.9 ±15.5^{a}	151.5 ±13.8	192.3 ± 9.8^{a,c}	-43.8^{x}	-4.4	-7.4	40.8^{x}

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a = significantly different from C2
b = significantly different from Pre
c = significantly different from Post 1
x = significantly different from Placebo
y = significantly different from Propranolol
z = significantly different from Atenolol

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